

CHAPTER 1

Esophageal disorders

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Question 1

A 47-year-old man with gastroesophageal reflux controlled with a daily proton pump inhibitor has an upper gastrointestinal endoscopy demonstrating Barrett's esophagus classified as C3M5 by Prague classification. Biopsies of the Barrett's esophagus demonstrate high-grade dysplasia confirmed by a second pathologist. On subsequent endoscopy, a 6 mm, raised lesion is detected at the 3-o'clock position, and the remainder of the mucosa appears consistent with flat Barrett's esophagus based on both white light endoscopy and narrow band imaging.

What is the next best step?

- A. Confirmatory esophageal biopsy
- B. Endoscopic mucosal resection
- C. Endoscopic ultrasound
- D. Proton pump inhibitor dose increase
- E. Radiofrequency ablation

CORRECT ANSWER: E

RATIONALE

Current Barrett's esophagus guidelines recommend resection of any raised lesions in the setting of Barrett's esophagus. More extensive endoscopic submucosal dissection is not necessary given the small nature of the raised lesion. Repeating the biopsy would not be beneficial, as the deeper margin can be assessed with endoscopic mucosal resection. Endoscopic ultrasound does not provide more information in the setting of dysplasia and would only be appropri-

ate if invasive malignancy was expected. Endoscopic ultrasound performs poorly with early esophageal cancers T1a/T1b but can be used to evaluate lymph node metastasis in those settings. Increasing the proton pump inhibitor dose will not treat the raised lesion. Radiofrequency ablation should be performed after resection of raised lesions or in the setting of flat Barrett's esophagus (ie, no raised lesions) with dysplasia. Typically, after the raised lesion is resected, endoscopic eradication therapy with ablation would be performed.

REFERENCES

American gastroenterological association medical position statement on the management of Barrett's esophagus. *Gastroenterology*. 2011;140(3):1084-1091. doi:10.1053/j.gastro.2011.01.030

Qumseya B, Sultan S, Bain P, et al. ASGE guideline on screening and surveillance of Barrett's esophagus. *Gastrointestinal Endoscopy*. 2019;90(3):335-359.e2. doi:10.1016/j.gie.2019.05.012

Question 2

A 62-year-old man with a history of mild heartburn undergoes an upper gastrointestinal endoscopy for evaluation of iron-deficiency anemia. He has a history of coronary artery disease, hypertension, diabetes, and obesity. His current medications include aspirin, enalapril, metformin, and glyburide. He also takes naproxen

twice weekly for joint pain. Endoscopy reveals erosive esophagitis (Los Angeles Grade C) and 3 cm of salmon-colored mucosa, proximal to the gastroesophageal junction. Biopsies are obtained and demonstrate evidence of chronic inflammation and indefinite dysplasia.

What is the most appropriate next step in management?

- A. Endoscopic mucosal resection
- B. Endoscopic ultrasound
- C. Naproxen discontinuation
- D. Proton pump inhibitor
- E. Radiofrequency ablation

CORRECT ANSWER: D

RATIONALE

In the setting of esophagitis and chronic inflammation, the diagnosis of dysplasia can be difficult to ascertain, often leading to a pathology read showing indefinite dysplasia. For someone who is not on a proton pump inhibitor, the next best step would be to start a proton pump inhibitor and repeat the upper gastrointestinal endoscopy with biopsy in 8 to 12 weeks to confirm dysplasia versus inflammation artifact. Endoscopic mucosal resection can be used to resect raised lesions demonstrating dysplasia or early esophageal malignancy without deep submucosal invasion, neither of which is present in this case. Endoscopic ultrasound is used to stage esophageal cancer and is not necessary in the setting of dysplasia or possible dysplasia. Rare naproxen use is not likely causing the esophagitis in this case and would not need to be discontinued. Although radiofrequency ablation is appropriate for flat Barrett's esophagus with dysplasia, it is unclear if the biopsy shows dysplasia or if this is an overcall in the setting of significant inflammation.

REFERENCE

Shaheen NJ, Falk GW, Iyer PG, Gerson LB. ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus. *American Journal of Gas-*

troenterology. 2016;111(1):30-50. doi:10.1038/ajg.2015.322

Question 3

A 62-year-old woman with 8 years of gastroesophageal reflux presents for a follow-up visit. She is currently taking omeprazole 40 mg daily, which is effective in eliminating heartburn symptoms. Her last upper gastrointestinal endoscopy was 18 months ago and demonstrated Prague classification C2M3 Barrett's esophagus without dysplasia on Seattle protocol biopsy of the salmon-colored mucosa. She does not smoke. She has lost 10 pounds over the past year intentionally through an exercise program and healthy eating.

What is the best estimate of her annual risk of Barrett's progressing to adenocarcinoma?

- A. 0.01%
- B. 0.1%
- C. 1%
- D. 5%
- E. 10%

CORRECT ANSWER: B

RATIONALE

The risk of progression to Barrett's esophagus in this patient is considered low. Based on the risk assessment score and population-based data, the risk is best estimated at approximately 0.1% annually. Based on the study by Parasa et al, noted below, the risk score is 3 (1 point/cm length of Barrett's esophagus), demonstrating a low risk of progression in Barrett's esophagus estimated at 0.13%.

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- Hvid-Jensen F, Pedersen L, Drewes M, Sci M, Sørensen HT, Funch-Jensen P. *Incidence of Adenocarcinoma among Patients with Barrett's Esophagus A B s t r A c t*. Vol 15.; 2011.
- Parasa S, Vennalaganti S, Gaddam S, et al. Development and Validation of a Model to Determine

Risk of Progression of Barrett's Esophagus to Neoplasia. *Gastroenterology*. 2018;154(5):1282-1289.e2. doi:10.1053/j.gastro.2017.12.009

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Question 4

A 52-year-old man with chronic gastroesophageal reflux disease presents for upper gastrointestinal (GI) endoscopy for Barrett's esophagus screening. He reports well-controlled symptoms of heartburn while on omeprazole 20 mg daily. He denies regurgitation, dysphagia, and weight loss. On upper GI endoscopy, you note the distal esophagus and gastroesophageal junction as per Figures 1 and 2.



Figure 1. White light endoscopy.

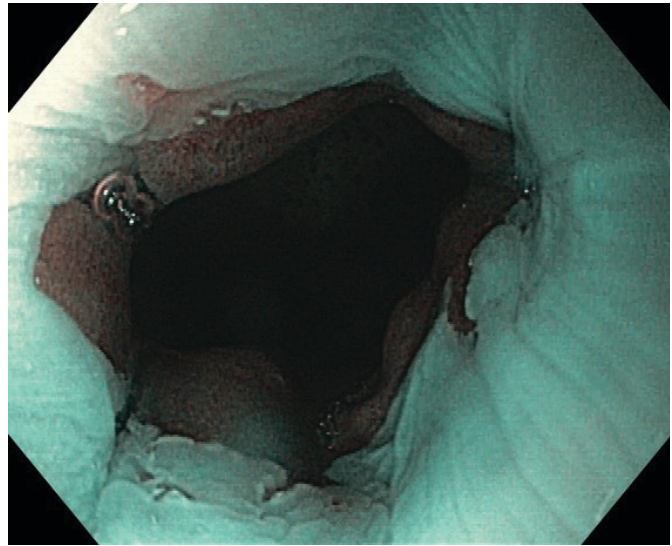


Figure 2. Narrow band imaging.

What is the next best step?

- A. Continue current regimen without changes
- B. Increase omeprazole to twice daily
- C. Repeat upper GI endoscopy in 3 years
- D. Perform 4-quadrant biopsy
- E. Refer for Nissen fundoplication

CORRECT ANSWER: A

RATIONALE

The photo shows an irregular Z line. Because the salmon-colored mucosa does not extend proximally for 1 cm, endoscopic appearance of Barrett's esophagus is not present; therefore, neither biopsy nor further recommendation for screening/surveillance is necessary. The patient is well controlled on the current regimen and has no evidence of esophagitis on endoscopy; therefore, increasing the omeprazole dose is not necessary. Although Nissen fundoplication could be considered, the patient is well controlled on low-dose omeprazole.

REFERENCE

Shaheen NJ, Falk GW, Iyer PG, Gerson LB. ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus. *American Journal of Gastroenterology*. 2016;111(1):30-50. doi:10.1038/ajg.2015.322

Question 5

A 72-year-old man with a history of only well-controlled hypertension and Barrett's esophagus (Prague classification C5M7) presents for surveillance upper gastrointestinal (GI) endoscopy. His last upper GI endoscopy was over 7 years ago, and biopsies at that time did not demonstrate dysplasia. Upper GI endoscopy reveals C6M7 Barrett's esophagus without visible abnormalities on white light endoscopy and narrow band imaging. Biopsies are taken using the Seattle protocol (4-quadrant biopsy every 2 cm). Pathology demonstrates columnar epithelium with Goblet cells without evidence of dysplasia.

What is the next best step in surveillance?

- A. Discontinue surveillance
- B. Repeat endoscopy in 6 months
- C. Repeat endoscopy in 1 year
- D. Repeat endoscopy in 3 years
- E. Repeat endoscopy in 7 years

CORRECT ANSWER: D

RATIONALE

Current guidelines for the management of Barrett's esophagus suggest surveillance at regular intervals but do not include a recommended age for discontinuing surveillance. In the setting of nondysplastic Barrett's esophagus, the current recommendation is to perform surveillance endoscopy within 3 to 5 years. The age at which to discontinue surveillance for Barrett's esophagus was recently studied in a comparative cost-effective analysis by Omidvari et al. It was found that for men with no, mild, moderate, and severe comorbidity, the optimal ages of last surveillance were 81, 80, 77, and 73 years, respectively.

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American gastroenterological association medical position statement on the management of Barrett's esophagus. *Gastroenterology*. 2011;140(3):1084-1091. doi:10.1053/j.gastro.2011.01.030

Omidvari AH, Hazelton WD, Lauren BN, et al. The Optimal Age to Stop Endoscopic Surveillance of Patients With Barrett's Esophagus Based on Sex and Comorbidity: A Comparative Cost-Effectiveness Analysis. *Gastroenterology*. 2021;161(2):487-494.e4. doi:10.1053/j.gastro.2021.05.003

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Question 6

A 55-year-old patient presents to discuss referral for upper gastrointestinal endoscopy for Barrett's esophagus screening. The patient describes chronic reflux symptoms that started at 38 years of age. The patient has no family history of Barrett's esophagus or esophageal cancer.

What additional risk factor would increase the patient's risk of Barrett's esophagus?

- A. Central obesity
- B. Female sex
- C. Hypertension
- D. Non-White race
- E. Work-related stress

CORRECT ANSWER: A

RATIONALE

The only risk factor listed in the answer choices is central obesity. Other risk factors for Barrett's esophagus include male sex, smoking history, age, chronic gastroesophageal reflux disease, and White race.

REFERENCES

American gastroenterological association medical position statement on the management of Barrett's esophagus. *Gastroenterology*. 2011;140(3):1084-1091. doi:10.1053/j.gastro.2011.01.030

Parasa S, Vennalaganti S, Gaddam S, et al. Development and Validation of a Model to Determine Risk of Progression of Barrett's Esophagus to Neoplasia. *Gastroenterology*. 2018;154(5):1282-1289. e2. doi:10.1053/j.gastro.2017.12.009

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Question 7

A 65-year-old man with long-standing history of Barrett's esophagus undergoes surveillance upper gastrointestinal endoscopy and is noted to have a 6 mm x 6 mm nodule at the 3 o'clock position. Biopsy demonstrated "at least high-grade dysplasia."

Which of the following will provide the best evidence for depth of tissue invasion?

- A. Confocal endomicroscopy
- B. Endoscopic mucosal resection
- C. Endoscopic ultrasonography
- D. Positron emission tomography
- E. Wide-area transepithelial sampling

CORRECT ANSWER: B

RATIONALE

In the setting of nodular Barrett's esophagus, the lesion is most likely high-grade dysplasia or early-stage esophageal adenocarcinoma. Endoscopic mucosal resection of the nodule will provide the most accurate evidence of tissue invasion, as the pathologic assessment can evaluate the mucosa and submucosal layers. Confocal endomicroscopy and wide-area transepithelial sampling are technologies that assess the mucosa and are not able to assess for depth of invasion. Endoscopic ultrasound can assess tissue invasion depth, but accuracy in dysplasia or early-stage esophageal adenocarcinoma (T1) is limited. Positron emission tomography is not able to ascertain tissue depth

but is used to evaluate for metastatic lesions in patients with esophageal malignancy.

REFERENCES

American gastroenterological association medical position statement on the management of Barrett's esophagus. *Gastroenterology*. 2011;140(3):1084-1091. doi:10.1053/j.gastro.2011.01.030

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Question 8

A 35-year-old man with a past medical history of gastroesophageal reflux disease undergoes an upper gastrointestinal endoscopy for evaluation of dysphagia. His only medication is omeprazole 20 mg daily. Biopsies of his esophagus demonstrate 40 eosinophils per high-power field in both the mid and distal esophagus. He would like to pursue a food elimination diet for treatment.

Which 6 food groups do you recommend eliminating?

- A. Banana/avocado, dairy, eggs, fish/shellfish, nuts, soy
- B. Banana/avocado, eggs, fish/shellfish, nuts, poultry, soy
- C. Eggs, fish/shellfish, nuts, oats, poultry, wheat
- D. Eggs, fish/shellfish, nuts, oats, soy, wheat
- E. Dairy, eggs, fish/shellfish, nuts, soy, wheat

CORRECT ANSWER: E

RATIONALE

The 6 food groups associated with eosinophilic esophagitis are dairy, eggs, fish/shellfish, nuts, soy, and wheat. Banana/avocado, oats, and poultry have not been implicated in eosinophilic esophagitis.

REFERENCE

Hirano I, Chan ES, Rank MA, et al. AGA Institute

and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. *Gastroenterology*. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038

Question 9

A 25-year-old man presents with episodes of “food slowing down after he swallows.” He notices this occurring most often with meats and rice but not with liquids. He states that his symptoms appear worse when he consumes alcoholic beverages. He denies heartburn symptoms. He recently had an episode that took several hours for his food to pass into his stomach and almost presented to the emergency department. He has a history of childhood asthma, mild eczema, and seasonal allergies but does not take any medications for these conditions.

What is the most likely diagnosis?

- A. Eosinophilic esophagitis
- B. Gastroesophageal reflux disease
- C. Hiatal hernia
- D. Peptic stricture
- E. Schatzki ring

CORRECT ANSWER: A

RATIONALE

This is a typical case of eosinophilic esophagitis in a young man presenting with dysphagia and a history of eczema, asthma, and allergies. In patients of this age group and with a history of asthma, eczema, and allergies, dysphagia is most often caused by eosinophilic esophagitis. Furthermore, without heartburn, gastroesophageal reflux disease and peptic stricture are unlikely to be the etiology. Given the presentation, the other possible diagnoses are far less likely.

REFERENCES

Hirano I, Chan ES, Rank MA, et al. AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the

Management of Eosinophilic Esophagitis. *Gastroenterology*. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038

Rank MA, Sharaf RN, Furuta GT, et al. Technical Review on the Management of Eosinophilic Esophagitis: A Report From the AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters. *Gastroenterology*. 2020;158(6):1789-1810.e15. doi:10.1053/j.gastro.2020.02.039

Question 10

A 38-year-old man presents with dysphagia to solid foods and undergoes upper gastrointestinal endoscopy, which shows esophageal edema, linear furrows, white plaques, and esophageal rings. Esophageal biopsies of both the proximal and distal esophagus demonstrate greater than 50 eosinophils per high-power field. After being treated with a proton pump inhibitor and swallowed topical steroids, a repeat endoscopy demonstrates improvement in the endoscopic findings and resolutions of the mucosal eosinophilia on biopsy. On follow-up, he continues to report dysphagia, and an upper gastrointestinal endoscopy notes persistent esophageal rings. An esophageal dilation to 15 mm is performed.

What is the most likely adverse outcome related to the procedure?

- A. Acute infection
- B. Contained perforation
- C. Postprocedural pain
- D. Significant bleeding
- E. Worsening reflux

CORRECT ANSWER: C

RATIONALE

Postprocedural pain after dilation in eosinophilic esophagitis is common, occurring in up to 74% in one study; however, many studies report lower rates of postprocedural pain. In a recent meta-

analysis, significant gastrointestinal bleeding occurred in 0.028%, perforation in 0.033%, and clinically significant chest pain in 3.64%. Acute infection and worsening reflux are unlikely to occur.

REFERENCES

Dougherty M, Runge TM, Eluri S, Dellon ES. Esophageal dilation with either bougie or balloon technique as a treatment for eosinophilic esophagitis: a systematic review and meta-analysis. *Gastrointestinal Endoscopy*. 2017;86(4):581-591.e3. doi:10.1016/j.gie.2017.04.028

Schoepfer AM, Gonsalves N, Bussmann C, et al. Esophageal dilation in eosinophilic esophagitis: Effectiveness, safety, and impact on the underlying inflammation. *American Journal of Gastroenterology*. 2010;105(5):1062-1070. doi:10.1038/ajg.2009.657

Question 11

A 35-year-old woman presented to you for dysphagia. An upper gastrointestinal endoscopy noted greater than 30 eosinophils per high-power field on mid- and distal-esophageal biopsy. She started a proton pump inhibitor twice daily without significant reduction in her eosinophil count on repeat biopsy. After 8 weeks of swallowed topical steroids (budesonide slurry 1 mg twice daily) and a proton pump inhibitor (omeprazole 40 mg daily), a repeat upper gastrointestinal endoscopy with biopsy revealed less than 5 eosinophils per high-power field. She continues swallowed topical budesonide for maintenance therapy.

What is the most likely adverse event to occur with her current medication regimen?

- A. Adrenal suppression
- B. Bone fracture
- C. Candida esophagitis
- D. Chronic kidney disease
- E. Hypomagnesemia

CORRECT ANSWER: C

RATIONALE

Candida esophagitis occurs in approximately 5% to 15% of individuals on swallowed topical steroids. Although adrenal suppression has rarely been reported in patients on swallowed topical steroids, these cases are predominantly in the pediatric population. Bone fracture, chronic kidney disease, and hypomagnesemia may occur with proton pump inhibitor use but are far less common than candida esophagitis in patients on swallowed topical steroids.

REFERENCES

Moayyedi P, Eikelboom JW, Bosch J, et al. Safety of Proton Pump Inhibitors Based on a Large, Multi-Year, Randomized Trial of Patients Receiving Rivaroxaban or Aspirin. *Gastroenterology*. 2019;157(3):682-691.e2. doi:10.1053/j.gastro.2019.05.056

Philpott H, Dougherty MK, Reed CC, et al. Systematic review: adrenal insufficiency secondary to swallowed topical corticosteroids in eosinophilic oesophagitis. *Alimentary Pharmacology and Therapeutics*. 2018;47(8):1071-1078. doi:10.1111/apt.14573

Schaefer ET, Fitzgerald JF, Molleston JP, et al. Comparison of Oral Prednisone and Topical Fluticasone in the Treatment of Eosinophilic Esophagitis: A Randomized Trial in Children. *Clinical Gastroenterology and Hepatology*. 2008;6(2):165-173. doi:10.1016/j.cgh.2007.11.008

Question 12

A 33-year-old man with a long-standing history of eosinophilic esophagitis presents for follow-up. His symptoms and esophageal eosinophilia are well controlled on a proton pump inhibitor and swallowed topical steroids. He denies dysphagia. He is interested in stopping medication therapy for his eosinophilic esophagitis and would like to start a food elimination diet.

Which of the following would you recommend for identifying his patient-specific food triggers?

- A. Empiric elimination diet
- B. Esophageal tissue staining
- C. Serum immunoglobulin E level
- D. Skin prick test
- E. Symptom correlation

CORRECT ANSWER: A

RATIONALE

Unfortunately, the most effective way to identify patient-specific food triggers is through an empiric elimination diet with reintroduction of food groups after histologic remission is attained. Esophageal tissue staining for allergens and/or immunoglobulins is currently in research trials. Allergy-based testing, including serum immunoglobulin E level and skin prick test, is not effective. Twelve single-arm studies reported that 49.2% of subjects on an allergy testing-based elimination diet failed to achieve histologic remission (defined as <15 eosinophils/high-power field). In randomized controlled trials involving patients with eosinophilic esophagitis, correlation between symptoms and histology was poor.

REFERENCES

Hirano I, Chan ES, Rank MA, et al. AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. *Gastroenterology*. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038

Molina-Infante J, Lucendo AJ. Dietary therapy for eosinophilic esophagitis. *Journal of Allergy and Clinical Immunology*. 2018;142(1):41-47. doi:10.1016/j.jaci.2018.02.028

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Question 13

A 47-year-old woman with mild asthma and seasonal allergies is seen for evaluation of dysphagia for the past 3 years. She notes food moving down her esophagus slowly, especially when she eats chicken and rice. She denies history of food impactions. She reports heartburn and takes calcium carbonate antacids as needed, typically several times weekly. She denies weight loss. On endoscopy, the esophagus has mucosal edema in the proximal esophagus and mucosal edema and longitudinal furrows in the distal esophagus. A 4 cm hiatal hernia is noted. Biopsies demonstrate 35 eosinophils per high-power field in the distal esophagus and 15 eosinophils per high-power field in the mid esophagus.

What is the best initial treatment for her condition?

- A. Antihistamine
- B. Esophageal dilation
- C. Food elimination diet
- D. Proton pump inhibitor
- E. Swallowed topical steroids

CORRECT ANSWER: D

RATIONALE

This is a case of eosinophilic esophagitis (EoE) based on esophageal dysfunction and esophageal eosinophilia greater than 15 eosinophils per high-power field, particularly in the setting of a person with asthma and seasonal allergies. The treatment of inflammation in EoE includes proton pump inhibitors (PPIs), swallowed topical steroids, food elimination, and, potentially, biologics. In this case, the best initial treatment is a PPI, which has a response rate of 30% to 50% in adults. For this case, modest esophageal eosinophilia is noted, with more eosinophilia in the distal esophagus, which may be more likely to respond to PPI therapy. Additionally, with the hiatal hernia and reflux symptoms, she likely has both gastroesophageal reflux disease and EoE; thus, a PPI is the best first choice. Given the overall availability, low cost, and

few side effects, PPIs are often the first choice in treatment of EoE, especially in individuals with heartburn symptoms. Antihistamine therapy does not reduce esophageal eosinophilia significantly. Esophageal dilation can be used to treat strictures and rings; however, it does not improve esophageal inflammation. A food elimination diet and swallowed topical steroids may be considered for some patients; therefore, individualized treatment of EoE with PPI, swallowed topical steroids, or food elimination diet based on patient preference and discussion of benefits/risks is reasonable.

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Hirano I, Chan ES, Rank MA, et al. AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. *Gastroenterology*. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038

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Molina-Infante J, Ferrando-Lamana L, Ripoll C, et al. Esophageal Eosinophilic Infiltration Responds to Proton Pump Inhibition in Most Adults. *Clinical Gastroenterology and Hepatology*. 2011;9(2):110-117. doi:10.1016/j.cgh.2010.09.019

Question 14

A 75-year-old woman is referred by her primary care doctor for evaluation of dysphagia. She reports intermittent dysphagia to dry foods for many years. She denies history of food impaction. She was recently seen in the otolaryngology clinic for plaques on her buccal mucosa that were biopsied and found to be benign findings. You perform an esophagogastroduodenoscopy, which demonstrates the esophageal findings in Figure 1.

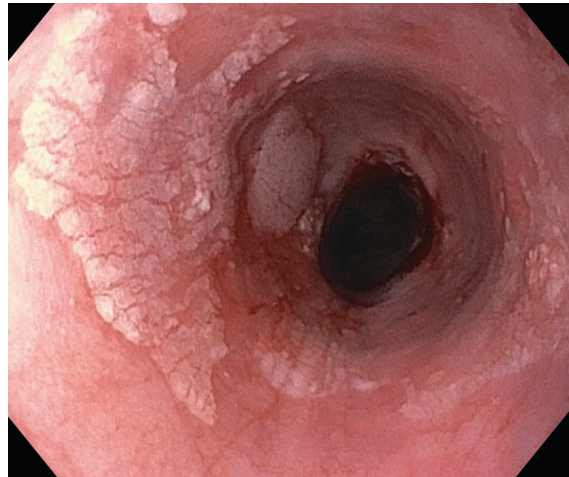


Figure 1. Esophageal findings on esophagogastroduodenoscopy.

What is the most likely diagnosis?

- A. Bullous pemphigoid
- B. Candida esophagitis
- C. Eosinophilic esophagitis
- D. Gastroesophageal reflux disease
- E. Lichen planus

CORRECT ANSWER: E

RATIONALE

The most likely diagnosis is lichen planus based on the plaques seen on endoscopy in the setting of a patient with oral plaques. Lichen planus is an idiopathic chronic inflammatory condition involving the skin, nails, and mucosal surfaces (including the esophageal mucosa). The endoscopic appearance is not consistent with bullous disease or candida esophagitis (white or yellow exudates). This photo does not have the classic appearance of eosinophilic esophagitis (edema, rings, furrows, exudates, and stricture), nor does it demonstrate erosive esophagitis as can be seen in gastroesophageal reflux disease, which typically occurs at the gastroesophageal junction extending proximally.

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Katzka DA, Smyrk TC, Bruce AJ, Romero Y, Alexander JA, Murray JA. Variations in pre-

sentations of esophageal involvement in lichen planus. *Clinical Gastroenterology and Hepatology*. 2010;8(9):777-782. doi:10.1016/j.cgh.2010.04.024

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Question 15

An 85-year-old man with hypertension, coronary artery disease, diabetes mellitus, and history of carotid endarterectomy presents to the clinic after having trouble swallowing for 3 weeks. He states he is unable to complete a full meal due to food not going down correctly. He notes coughing when he swallows and often stops eating after a few bites. He reports weight loss of 4 pounds.

What is the next best step?

- A. Esophageal manometry
- B. Modified barium swallow
- C. Otolaryngology referral
- D. Proton pump inhibitor
- E. Upper gastrointestinal endoscopy

CORRECT ANSWER: B

RATIONALE

Coughing while eating likely indicates oropharyngeal dysphagia. In this case, a patient with hypertension, coronary artery disease, diabetes mellitus, and history of carotid endarterectomy make an ischemic stroke a likely etiology. The best test to evaluate oropharyngeal dysphagia is a modified barium swallow. The oropharyngeal nature of the symptoms makes esophageal

dysmotility less likely; thus, esophageal manometry would not be indicated. Otolaryngology can assist in oropharyngeal diseases but would have little additional diagnostic or treatment options to offer if the patient's symptoms are due to uncoordinated swallow mechanism. A trial of a proton pump inhibitor is unlikely to be helpful for oropharyngeal dysphagia. Upper gastrointestinal endoscopy can be used to rule out structural and mucosal esophageal diseases in individuals with dysphagia but is less likely to be helpful in a case of oropharyngeal dysphagia.

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Cook IJ. Diagnostic evaluation of dysphagia. *Nature Clinical Practice Gastroenterology and Hepatology*. 2008;5(7):393-403. doi:10.1038/npcgasthep1153

Malagelada JR, Bazzoli F, Elewaut A, et al. *World Gastroenterology Organisation Practice Guidelines: Dysphagia Review Team*.

Question 16

A 77-year-old man presents with trouble swallowing and a skin rash on his hands and around his eyelids. He reports infrequent heartburn occurring approximately once monthly, which is relieved with calcium carbonate antacids. His trouble swallowing has been intermittent and occurs with both liquids and solids. He has also noticed difficulty in climbing stairs and getting up from his chair. On examination, he has good dentition and a pink-violaceous erythema overlying his interphalangeal and metacarpophalangeal joints and involving his periorbital skin. He also has weakness in his hip flexor muscles. Laboratory tests show a creatine kinase level of 3000 IU/L (reference range, 55–170 U/L). Tests for antinuclear antibody (ANA) and small ubiquitin-like modifier activating enzyme (anti-SAE) antibody are both positive.

What is the most likely reason for the patient's trouble swallowing?

- A. Achalasia
- B. Distal esophageal spasm
- C. Gastroesophageal reflux disease
- D. Myositis
- E. Zenker's diverticulum

CORRECT ANSWER: D

RATIONALE

This is a case of dermatomyositis presenting with skin rash and proximal muscle weakness. The elevated creatine kinase level and positive ANA and anti-SAE antibody tests confirm the likely diagnosis. In cases of dermatomyositis, the most likely reason for trouble swallowing is oropharyngeal dysphagia. His trouble swallowing is less likely related to esophageal disorders (achalasia, esophageal spasm, Zenker's diverticulum) given the association of dermatomyositis and oropharyngeal dysphagia. He does not report symptoms associated with reflux, making gastroesophageal reflux disease less likely.

REFERENCE

Labeit B, Pawlitzki M, Ruck T, et al. The Impact of Dysphagia in Myositis: A Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*. 2020;9(7):2150. doi:10.3390/jcm9072150

Question 17

A 24-year-old woman presents to the emergency department with chest pain for 2 days. She has a history of seasonal allergies, acne, and well-controlled asthma. A cardiac evaluation reveals no evidence of ischemia. She denies history of heartburn and regurgitation. An upper gastrointestinal endoscopy is performed and demonstrates ulceration at 33 cm from the incisors. The Z line is normal at 40 cm from the incisors.

What medication is most likely to be the etiology of her esophagitis?

- A. Doxycycline
- B. Fluoxetine

- C. Methylphenidate
- D. Oral contraceptive
- E. Retinol

CORRECT ANSWER: A

RATIONALE

In this patient without history of gastrointestinal reflux disease, heartburn, or regurgitation, the most likely etiology of mid-esophageal ulceration in pill-induced esophagitis. A young person with acne may be prescribed an antibiotic (doxycycline), which makes this the most likely etiology. The most likely etiologies of pill-induced esophagitis include antibiotics, nonsteroidal antiinflammatory drugs, and bisphosphonates. The other medications are not known to cause esophagitis.

REFERENCES

Kim SH, Jeong JB, Kim JW, et al. Clinical and endoscopic characteristics of drug-induced esophagitis. *World Journal of Gastroenterology*. 2014;20(31):10994-10999. doi:10.3748/wjg.v20.i31.10994

Zografos GN, Georgiadou D, Thomas D, Katsas G, Digalakis M. Drug-induced esophagitis. *Diseases of the Esophagus*. 2009;22(8):633-637. doi:10.1111/j.1442-2050.2009.00972.x

Question 18

A 68-year-old woman with chest pain is seen in the emergency department. She has a history of hypertension, hypothyroidism, diabetes, and osteoporosis. She denies heartburn. An electrocardiogram is performed and demonstrates normal rate and rhythm without other abnormalities. The troponin level is normal. Computed tomography is performed and shows no acute abnormalities in the chest or abdomen. An endoscopy is performed and demonstrates esophageal ulceration at 33 cm from the incisors. The Z line is regular without erythema or erosions at 39 cm from the incisors. The remainder of the upper gastrointestinal endoscopy is normal.

What is the most likely etiology of her esophageal ulceration?

- A. Eosinophilic esophagitis
- B. Gastroesophageal reflux disease
- C. Ischemic esophagitis
- D. Pill-induced esophagitis
- E. Viral esophagitis

CORRECT ANSWER: D

RATIONALE

The most likely etiology of mid-esophageal ulceration without evidence of distal esophagitis is pill-induced esophagitis. The most likely etiologies of pill-induced esophagitis include antibiotics, nonsteroidal antiinflammatory drugs, and bisphosphonates. Given the patient's history of osteoporosis, the most likely etiology of her ulcerations is a bisphosphonate. Eosinophilic esophagitis does not typically present with ulceration. Gastroesophageal reflux disease can cause erosive esophagitis starting at the gastroesophageal junction but does not cause ulcerations more proximally without involvement of the distal esophagus. Ischemic esophagitis is unlikely given the clinical history. Viral esophagitis can have ulceration, but the patient is not immunosuppressed, so this would be less likely.

REFERENCES

Kim SH, Jeong JB, Kim JW, et al. Clinical and endoscopic characteristics of drug-induced esophagitis. *World Journal of Gastroenterology*. 2014;20(31):10994-10999. doi:10.3748/wjg.v20.i31.10994

Zografos GN, Georgiadou D, Thomas D, Kaltsas G, Digalakis M. Drug-induced esophagitis. *Diseases of the Esophagus*. 2009;22(8):633-637. doi:10.1111/j.1442-2050.2009.00972.x

Question 19

An 81-year-old man presents with trouble swallowing, throat clearing, and occasional cough particularly during and shortly after eating. He often feels

like he regurgitates food and can “taste” food from the day before. He has a history of hypertension, coronary artery disease, and diabetes mellitus.

An esophagram is performed with representative images below.



What is the most likely diagnosis?

- A. Esophageal dysmotility
- B. Esophageal web
- C. Extrinsic compression
- D. Neurodegenerative dysphagia
- E. Zenker's diverticulum

CORRECT ANSWER: E

RATIONALE

The esophagram demonstrates a Zenker's diverticulum. A Zenker's diverticulum is a sac-like out-

pouching of the mucosa and submucosa through Killian's triangle, an area of muscular weakness between the transverse fibers of the cricopharyngeus muscle and the oblique fibers of the lower inferior constrictor muscle. This is typically seen in patients in their seventh or eighth decade of life and presents with regurgitation, halitosis, and dysphagia. Esophageal dysmotility, esophageal web, and extrinsic compression are not demonstrated on the figure. An esophagram can show tracheal aspiration or penetration in oropharyngeal dysphagia, which is often secondary to neurodegenerative diseases, but this is also not demonstrated in the images.

REFERENCE

Law R, Katzka DA, Baron TH. Zenker's Diverticulum. *Clinical Gastroenterology and Hepatology*. 2014;12(11):1773-1782. doi:10.1016/j.cgh.2013.09.016

Question 20

A 77-year-old woman with a history of lung cancer treated with chemotherapy, radiation, and partial lung resection 15 years ago presents with trouble swallowing, which has been slowly progressing over the past 2 years. Food gets stuck intermittently. She denies issues with liquids. Typical foods that get stuck include breads and meats. She denies heartburn, regurgitation, and hoarseness in her voice.

What is the most likely etiology of her dysphagia?

- A. Eosinophilic esophagitis
- B. Esophageal dysmotility
- C. Esophageal malignancy
- D. Peptic stricture
- E. Radiation-induced stricture

CORRECT ANSWER: E

RATIONALE

The most likely etiology of her dysphagia is radiation-induced esophagitis, which can be

early or late onset, given her history of radiation. Eosinophilic esophagitis is less likely in an elderly patient without underlying history of asthma, eczema, or allergies. Esophageal dysmotility typically causes issues with solids and liquids. Although esophageal malignancy is possible, a radiation-induced stricture is more likely given the slowly progressing nature of the dysphagia. A peptic stricture is less likely due to a lack of heartburn or regurgitation.

REFERENCE

McCaughan H, Boyle S, McGoran JJ. Update on the management of the gastrointestinal effects of radiation. *World Journal of Gastrointestinal Oncology*. 2021;13(5):400-408. doi:10.4251/wjgo.v13.i5.400

Question 21

A 65-year-old man presents with intermittent solid-food dysphagia for several years. He states that, occasionally, meat is "hung up" in his esophagus but passes into his stomach after 30 to 60 minutes. He denies weight loss. He rarely experiences heartburn. An esophagram demonstrates the finding in Figure 1. Upper gastrointestinal endoscopy reveals the finding in Figure 2.



Figure 1. Esophagram finding.

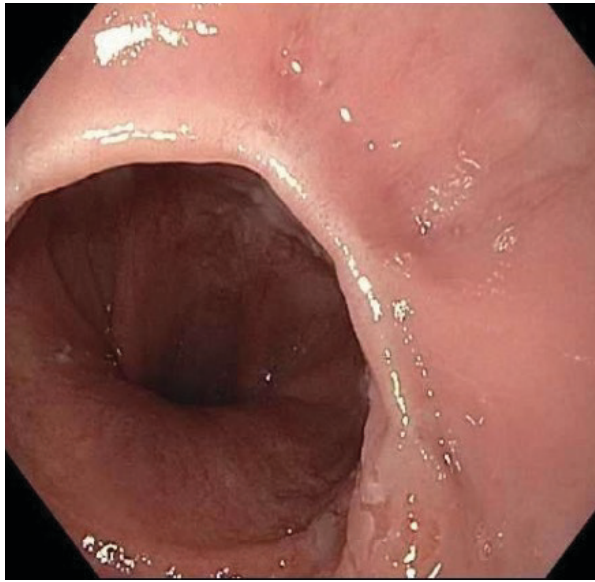


Figure 2. Upper gastrointestinal endoscopy finding.

What is the next best step in management?

- A. Balloon dilation
- B. Food elimination diet
- C. Metal stent placement
- D. Nissen fundoplication
- E. Steroid injection

CORRECT ANSWER: A

RATIONALE

The endoscopic image shows a Schatzki ring in the setting of a small hiatal hernia. The most important management is to disrupt the ring of tissue, which can be done via balloon dilation. Other possible methods of disruption of the ring include tissue biopsy and cautery using a needle knife; however, the majority of Schatzki rings respond adequately to balloon dilation. Food elimination diets can be used to treat eosinophilic esophagitis. Metal stents have been used in refractory esophageal strictures, but an initial presentation of a Schatzki ring is not considered refractory and would not warrant stent placement. A Nissen fundoplication is not indicated and may make dysphagia worse. Steroid injection has been reported in esophageal stricture treatment, but not in Schatzki ring.

REFERENCE

Jalil S, Castell D. Schatzki's Ring. *Journal of Clinical Gastroenterology*. 2002;35:295-298. Doi:10.1097/00004836-200210000-00004

Question 22

A 65-year-old man undergoes an upper gastrointestinal endoscopy for evaluation of iron deficiency anemia. He denies heartburn, abdominal pain, regurgitation, and globus sensation. His distal esophagus is normal in appearance with a regular Z line at 39 cm from the incisors. On withdrawal, you notice the lesion below at 18 cm from the incisors.

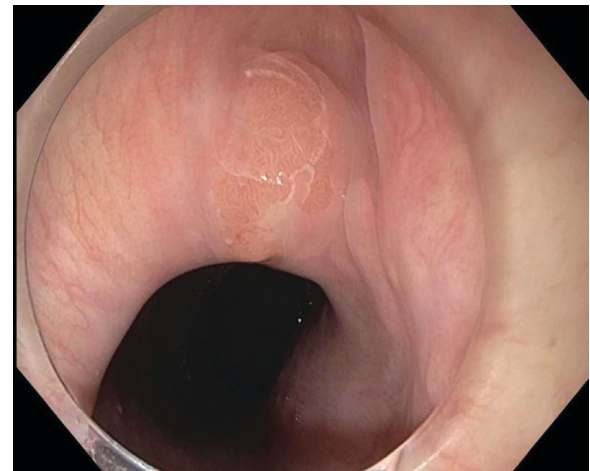


Figure 1. White light endoscopy.

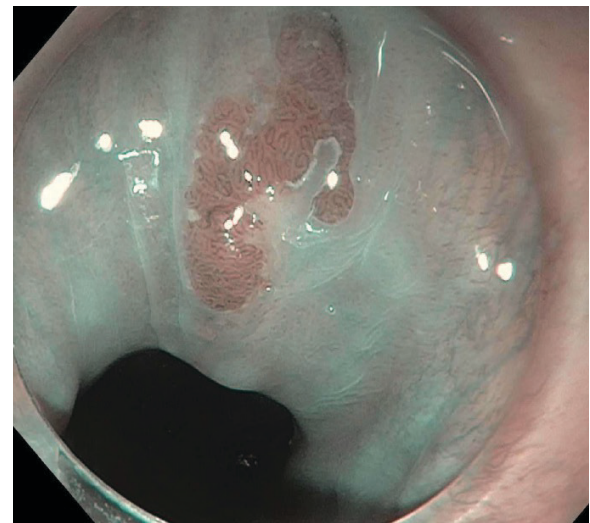


Figure 2. Narrow band imaging.

What is the appropriate therapy?

- A. Argon plasma coagulation ablation
- B. Endoscopic mucosal resection
- C. No further therapy
- D. Proton pump inhibitor
- E. Radiofrequency ablation

CORRECT ANSWER: C

RATIONALE

The photo demonstrates an inlet patch, otherwise known as heterotopic gastric mucosa of the upper esophagus. Inlet patches range in size from 2 mm to 4.5 cm and can be solitary or multiple. Most inlet patches are found incidentally and do not cause symptoms. Because most are asymptomatic, further therapy is not necessary. Argon plasma coagulation and radiofrequency ablation have been reported as a potential treatment of globus sensation in individuals with inlet patches, but this patient does not report a globus sensation. Endoscopic mucosal resection is not necessary and has some risks to it that would be unwarranted for an asymptomatic benign lesion such as this. Proton pump inhibitor therapy will not treat an inlet patch and in the absence of symptoms of gastroesophageal reflux disease is unnecessary.

REFERENCE

Jacobs E, Dehou MF. Heterotopic gastric mucosa in the upper esophagus: A prospective study of 33 cases and review of literature. *Endoscopy*. 1997;29(8). doi:10.1055/s-2007-1004294

Question 23

A 52-year-old woman is seen in clinic for evaluation of dysphagia. She denies heartburn and reflux. Her only medication is levothyroxine. An upper gastrointestinal endoscopy is performed and demonstrates concentric rings, mucosal edema, and a narrowed esophagus. Scope passage caused a small mucosal rent. The stomach and small bowel appeared normal. Biopsies of the esophagus demonstrate greater than 50 peripap-

illary lymphocytes with a few eosinophils (2-3/high-power field).

What is the most likely diagnosis?

- A. Caustic ingestion
- B. Eosinophilic esophagitis
- C. Gastroesophageal reflux disease
- D. Lichen planus
- E. Lymphocytic esophagitis

CORRECT ANSWER: E

RATIONALE

Lymphocytic esophagitis should be considered when evaluating dysphagia, although it is rare and found in only 0.09% of esophageal biopsies. It is unclear if lymphocytic esophagitis is an independent entity or closely related to gastroesophageal reflux disease, eosinophilic esophagitis, or allergic diseases. The diagnosis is made based on histology, whereby intraepithelial lymphocytes are seen on esophageal biopsy with few or no intraepithelial granulocytes or eosinophils. There is nothing in this case to suggest caustic ingestion. The diagnosis of eosinophilic esophagitis requires greater than 15 eosinophils per high-power field. Gastroesophageal reflux disease is unlikely given the lack of heartburn or reflux symptoms and the presence of significant lymphocytes on biopsies. Lichen planus esophagus can present with a varied endoscopic appearance, including white plaques, edema, or narrowed esophagus and stricturing but not concentric rings. The characteristic histopathologic sign is the presence of Civette bodies, which represent degenerating basal cells caused by autoimmune T-cell-mediated damage.

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Jacobs, J, Kukreja, K, Camisa, C, Richter, J. Demystifying Esophageal Lichen Planus: A Comprehensive Review of a Rare Disease You Will See in Practice. *Am J Gastroenterol* 2021;00:1–8.

Nguyen AD, Dunbar KB. How to Approach Lymphocytic Esophagitis. *Current Gastroenterology Re-*

ports. 2017;19(6). doi:10.1007/s11894-017-0564-y

Question 24

A 63-year-old woman is admitted to the hospital with nausea and odynophagia. She underwent bone marrow transplant 6 months ago. An upper gastrointestinal endoscopy shows multiple small (<5 mm), shallow ulcerations in the esophagus from 33 to 36 cm from the incisors. A slight yellow exudate is present on several of the ulcerations. Biopsies demonstrate multinucleated giant cells.

What is the most likely diagnosis?

- A. Candida esophagitis
- B. Eosinophilic esophagitis
- C. Peptic esophagitis
- D. Pill-induced esophagitis
- E. Viral esophagitis

CORRECT ANSWER: E

RATIONALE

Viral esophagitis (herpes esophagitis) is the most likely etiology when esophageal ulcerations are noted in the presence of multinucleated giant cells. Candida esophagitis and eosinophilic esophagitis do not typically cause esophageal ulcerations. Peptic esophagitis is seen at the gastroesophageal junction progressing proximally. Pill-induced esophagitis occurs most often with antibiotics, nonsteroidal antiinflammatory drugs, and bisphosphonates.

REFERENCES

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McBane RD, Gross JB. Herpes esophagitis: clinical syndrome, endoscopic appearance, and

diagnosis in 23 patients. *Gastrointestinal Endoscopy*. 1991;37(6):600-603. doi:10.1016/S0016-5107(91)70862-6

Question 25

A 33-year-old woman is seen in the clinic for evaluation of trouble swallowing, which she first noticed several years ago. She states that she feels like something is constantly in the back of her throat. It is not painful and is less noticeable while she is eating. She denies food getting stuck in her esophagus or slowing down after she swallows. She denies painful swallowing, weight loss, heartburn, and regurgitation. Approximately 3 months ago, she had an upper gastrointestinal endoscopy and esophageal manometry, which were both normal.

What is the most likely diagnosis?

- A. Eosinophilic esophagitis
- B. Esophageal dysmotility
- C. Functional heartburn
- D. Gastroesophageal reflux disease
- E. Globus pharyngeus

CORRECT ANSWER: E

RATIONALE

This presentation demonstrates a typical case of globus sensation that meets the criteria including presence of persistent, nonpainful sensation in the throat without structural lesions, occurrence of symptoms between meals, absence of dysphagia or odynophagia, and absence of a gastric inlet patch. The mainstay of treatment for globus sensation remains explanation and reassurance. No evidence (symptomatically and endoscopically) of eosinophilic esophagitis or gastroesophageal reflux disease is present. Esophageal manometry ruled out major esophageal motor disorders. This is not functional heartburn since she has no complaints of heartburn. According to Rome IV criteria, a diagnosis of functional heartburn can be made when the following criteria are pres-

ent for the last 3 months: burning retrosternal discomfort or pain, absence of symptom relief despite optimal antisecretory therapy, absence of evidence that gastroesophageal reflux or eosinophilic esophagitis are the cause of symptoms, and absence of major esophageal motor disorders.

REFERENCE

Aziz Q, Fass R, Gyawali CP, Miwa H, Pandolfino JE, Zerbib F. Esophageal disorders. *Gastroenterology*. 2016;150(6):1368-1379. doi:10.1053/j.gastro.2016.02.012

Question 26

A 35-year-old woman is referred to you for 2 years of heartburn that has progressed to a daily occurrence. She denies regurgitation, chest pain, sore throat, and cough. Her body mass index is 21 kg/m². She reports no dysphagia, unintentional weight loss, or gastrointestinal (GI) bleeding. A recent complete blood count was normal. She has never tried any pharmacotherapy for her symptoms.

What is the next best step?

- A. Ambulatory reflux monitoring
- B. Low-dose antidepressant trial
- C. Nissen fundoplication
- D. Proton pump inhibitor
- E. Upper GI endoscopy

CORRECT ANSWER: D

RATIONALE

This presentation represents typical symptoms of gastroesophageal reflux disease (GERD) without warning signs or symptoms, for which an 8-week trial of single-dose proton pump inhibitor (PPI) therapy is recommended. Ambulatory reflux monitoring is recommended once erosive reflux disease has been excluded in a patient who did not derive symptom response with PPI therapy. Antireflux surgery such as Nissen fundoplication should be considered only in patients with

established objective GERD. Antidepressants are a treatment option for patients diagnosed with functional heartburn or reflux hypersensitivity. Evaluation with upper GI endoscopy would be recommended if warning signs or symptoms (dysphagia, weight loss, anemia, signs of upper GI bleeding) were present and/or if the patient did not derive symptom response with PPI therapy.

REFERENCES

Gyawali CP, Carlson DA, Chen JW, Patel A, Wong RJ, Yadlapati RH. ACG Clinical Guidelines: Clinical Use of Esophageal Physiologic Testing. *Am J Gastroenterol*. 2020;115(9):1412-1428. doi:10.14309/ajg.0000000000000734

Gyawali CP, Kahrilas PJ, Savarino E, et al. Modern diagnosis of GERD: the Lyon Consensus. *Gut*. 2018;67(7):1351-1362. doi:10.1136/gutjnl-2017-314722

Question 27

A 23-year-old man is referred to you for regurgitation and mild heartburn. Regurgitation occurs daily and includes nocturnal regurgitation, which wakes him from sleep. He has also noticed progressively worsening dysphagia to solids and pills. He denies weight loss. He has not trialed any medications for his symptoms and has not had any prior testing.

What is the next best step?

- A. Ambulatory reflux monitoring
- B. Dietary and sleep position modifications
- C. Nissen fundoplication
- D. Proton pump inhibitor
- E. Upper gastrointestinal endoscopy

CORRECT ANSWER: E

RATIONALE

This presentation represents typical symptoms of gastroesophageal reflux disease (GERD) with

a warning sign of dysphagia. Warning signs of erosive reflux disease or other pathology such as eosinophilic esophagitis, structuring disease or malignancy include dysphagia, upper gastrointestinal bleeding, anemia, and weight loss. Evaluation with upper gastrointestinal endoscopy is recommended when warning signs or symptoms are present. A proton pump inhibitor would be appropriate in the absence of warning signs or symptoms. Ambulatory reflux monitoring is recommended once erosive reflux disease has been excluded in a patient who did not derive symptom response with proton pump inhibitor therapy. Antireflux surgery such as Nissen fundoplication should only be considered in patients with established objective GERD. Although dietary and sleep position modifications can be recommended to any patient with suspected GERD, they are not the next best step for this patient with warning signs.

REFERENCES

Gyawali CP, Carlson DA, Chen JW, Patel A, Wong RJ, Yadlapati RH. ACG Clinical Guidelines: Clinical Use of Esophageal Physiologic Testing. *Am J Gastroenterol*. 2020;115(9):1412-1428. doi:10.14309/ajg.0000000000000734

Gyawali CP, Kahrilas PJ, Savarino E, et al. Modern diagnosis of GERD: the Lyon Consensus. *Gut*. 2018;67(7):1351-1362. doi:10.1136/gutjnl-2017-314722

Question 28

A 45-year-old woman is referred by her otolaryngologist for dysphonia and sore throat. She has experienced these laryngeal symptoms for 1 year. She denies symptoms of heartburn and regurgitation. She has no dysphagia, unintentional weight loss, anemia, or gastrointestinal bleeding.

She is a nonsmoker. A recent flexible laryngoscopic examination was unrevealing, and she was told that laryngopharyngeal reflux may be a cause of her symptoms.

What is the next best step?

- A. Ambulatory reflux monitoring
- B. Low-dose antidepressant
- C. Nissen fundoplication
- D. Proton pump inhibitor
- E. Speech and swallow therapy

CORRECT ANSWER: A

RATIONALE

This presentation represents extraesophageal symptoms in the absence of typical reflux symptoms and absence of warning signs or symptoms. The pretest probability of laryngopharyngeal reflux is low in this patient, and the next best step is objective evaluation for gastroesophageal reflux disease with ambulatory reflux monitoring before a trial of proton pump inhibitor therapy. Antireflux surgery such as Nissen fundoplication should only be considered in patients with established objective gastroesophageal reflux disease.

Low-dose antidepressants and/or speech and swallow therapy can be considered once laryngeal hypersensitivity or a functional process has been diagnosed via reflux monitoring.

REFERENCE

Gyawali CP, Carlson DA, Chen JW, Patel A, Wong RJ, Yadlapati RH. ACG Clinical Guidelines: Clinical Use of Esophageal Physiologic Testing. *Am J Gastroenterol*. 2020;115(9):1412-1428. doi:10.14309/ajg.0000000000000734

Question 29

A 66-year-old man undergoes an upper gastrointestinal endoscopy for 6 months of progressively worsening dysphagia to solid foods and pills. Upper gastrointestinal endoscopy reveals multiple mucosal breaks that extend 3 cm proximal to the squamocolumnar junction and involve 50% of the circumference.

How would you classify these findings?

- A. Los Angeles B esophagitis
- B. Los Angeles C esophagitis
- C. Los Angeles D esophagitis
- D. Prague C1M3 Barrett's esophagus
- E. Prague C3M3 Barrett's esophagus

CORRECT ANSWER: B

RATIONALE

This case represents an endoscopic presentation of Los Angeles C esophagitis. Los Angeles B esophagitis is defined as 1 or more mucosal break(s) more than 5 mm long that do(es) not extend between the tops of 2 mucosal folds. Los Angeles C esophagitis is defined as 1 or more mucosal break(s), continuous between the tops of 2 or more mucosal folds, which involve(s) less than 75% of the circumference. Los Angeles D esophagitis is defined as 1 or more mucosal break(s), which involve(s) at least 75% of the esophageal circumference. A diagnosis of Barrett's esophagus requires histologic confirmation of intestinal metaplasia and should be diagnosed in the absence of mucosal breaks/esophagitis.

REFERENCES

Gyawali CP, Carlson DA, Chen JW, Patel A, Wong RJ, Yadlapati RH. ACG Clinical Guidelines: Clinical Use of Esophageal Physiologic Testing. *Am J Gastroenterol*. 2020;115(9):1412-1428. doi:10.14309/ajg.0000000000000734

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Lundell LR, Dent J, Bennett JR, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut*. 1999;45(2):172-180. doi:10.1136/gut.45.2.172

Question 30

A 68-year-old woman undergoes an upper gastro-

intestinal endoscopy for 3 months of dysphagia to solids, heartburn, and regurgitation. Upper gastrointestinal endoscopy reveals Los Angeles D esophagitis.

What is the next best step?

- A. 4-quadrant biopsies of esophagitis every 1-2 cm
- B. Ambulatory reflux monitoring
- C. Double-dose proton pump inhibitor therapy
- D. Esophageal high-resolution manometry
- E. H2 receptor blocker therapy

CORRECT ANSWER: C

RATIONALE

This presentation represents severe erosive reflux disease for which double-dose proton pump inhibitor therapy for 8 weeks is recommended followed by an upper endoscopy to evaluate for healing of the esophagitis and surveillance for potential underlying Barrett's esophagus. In the setting of esophagitis, 4-quadrant biopsies are not indicated and can yield a false-positive diagnosis of intestinal metaplasia (Barrett's esophagus). Ambulatory reflux monitoring would be indicated to evaluate for nonerosive reflux disease. However, this case demonstrates erosive esophagitis indicative of gastroesophageal reflux disease; thus, ambulatory reflux monitoring is unnecessary. Since the etiology of dysphagia is identified, esophageal manometry is not indicated. H2 receptor antagonists are not very effective at healing erosive esophagitis but may be used for mild symptoms of gastroesophageal reflux disease in the absence of esophagitis.

REFERENCES

Gyawali CP, Carlson DA, Chen JW, Patel A, Wong RJ, Yadlapati RH. ACG Clinical Guidelines: Clinical Use of Esophageal Physiologic Testing. *Am J Gastroenterol*. 2020;115(9):1412-1428. doi:10.14309/ajg.0000000000000734

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Wang WH, Huang JQ, Zheng GF, et al. Head-to-head comparison of H2-receptor antagonists and proton pump inhibitors in the treatment of erosive esophagitis: a meta-analysis. *World J Gastroenterol*. 2005;11(26):4067-4077. doi:10.3748/wjg.v11.i26.4067

Question 31

A 35-year-old woman undergoes upper gastrointestinal endoscopy for evaluation of troublesome heartburn that did not respond to an 8-week trial of proton pump inhibitor therapy. Upper gastrointestinal endoscopy shows no erosive esophagitis or peptic stricture. The squamocolumnar junction is regular without proximal extension of columnar-lined mucosa. You proceed with 96-hour wireless pH monitoring off proton pump inhibitor therapy, which reveals physiologic acid exposure time (<4.0%) on all 4 days of monitoring and a negative symptom reflux association.

Which of the following is the most likely diagnosis?

- A. Achalasia
- B. Barrett's esophagus
- C. Erosive reflux disease
- D. Functional heartburn
- E. Nonerosive reflux disease

CORRECT ANSWER: D

RATIONALE

This presentation represents functional heartburn, which is defined in the Rome IV criteria as typical heartburn symptoms in the presence of normal upper endoscopy findings, normal am-

bulatory reflux testing, and negative association between symptoms and reflux events. Achalasia is an esophageal motor disorder characterized by inadequate relaxation of the lower esophageal sphincter and absence of peristalsis. Barrett's esophagus requires the presence of salmon-colored mucosa in the esophagus with histologic confirmation of intestinal metaplasia. Erosive reflux disease includes severe erosive esophagitis, long-segment Barrett's esophagus, or peptic stricture on upper gastrointestinal endoscopy. Nonerosive reflux disease is defined as elevated acid exposure on ambulatory reflux monitoring in the presence of normal upper endoscopy findings.

REFERENCES

Aziz Q, Fass R, Gyawali CP, Miwa H, Pandolfino JE, Zerbib F. Functional Esophageal Disorders [published online ahead of print, 2016 Feb 15]. *Gastroenterology*. 2016;S0016-5085(16)00178-5. doi:10.1053/j.gastro.2016.02.012

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Question 32

A 42-year-old man undergoes upper gastrointestinal endoscopy for evaluation of troublesome heartburn and chest pain that did not respond to an 8-week trial of proton pump inhibitor

therapy. Upper gastrointestinal endoscopy shows no erosive esophagitis or peptic stricture. The squamocolumnar junction is regular without proximal extension of columnar-lined mucosa. You proceed with 96-hour wireless pH monitoring off proton pump inhibitor therapy, which reveals pathologic acid exposure time (>6.0%) overall with elevated acid exposure across all 4 days of monitoring. More than 50% of heartburn symptoms reported are associated with an acid reflux event with a positive symptom association probability.

Which of the following is the most likely diagnosis?

- A. Achalasia
- B. Barrett's esophagus
- C. Erosive reflux disease
- D. Functional heartburn
- E. Nonerosive reflux disease

CORRECT ANSWER: E

RATIONALE

This presentation represents nonerosive reflux disease, which is defined as elevated acid exposure on ambulatory reflux monitoring in the presence of normal upper endoscopy findings. Achalasia is an esophageal motor disorder characterized by inadequate relaxation of the lower esophageal sphincter and absence of peristalsis. Barrett's esophagus requires the presence of salmon-colored mucosa in the esophagus with histologic confirmation of intestinal metaplasia. Erosive reflux disease includes severe erosive esophagitis, long-segment Barrett's esophagus, or peptic stricture on upper gastrointestinal endoscopy. Functional heartburn is defined in the Rome IV criteria as typical heartburn symptoms in the presence of normal upper endoscopy findings, normal ambulatory reflux testing, and negative association between symptoms and reflux events.

REFERENCES

Aziz Q, Fass R, Gyawali CP, Miwa H, Pandolfino

JE, Zerbib F. Functional Esophageal Disorders [published online ahead of print, 2016 Feb 15]. *Gastroenterology*. 2016;S0016-5085(16)00178-5. doi:10.1053/j.gastro.2016.02.012

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Question 33

A 35-year-old man with 1 year of heartburn that did not respond to proton pump inhibitor (PPI) therapy undergoes upper gastrointestinal endoscopy and 96-hour wireless pH monitoring. Diagnostic testing is consistent with functional heartburn. The patient denies chest pain, weight loss, and regurgitation.

What is the next best step in management?

- A. Dietary and sleep position modifications
- B. Escalation to double-dose PPI therapy
- C. Esophageal high-resolution manometry
- D. Low-dose antidepressant trial
- E. Nissen fundoplication

CORRECT ANSWER: D

RATIONALE

The recommended management of functional heartburn is neuromodulation in the form of a

low-dose antidepressant and/or behavioral therapy. In addition, PPI therapy should be tapered off as tolerated. Antireflux surgery such as Nissen fundoplication is not indicated for functional heartburn. Dietary and sleep position modifications are recommended in the setting of gastroesophageal reflux disease, which this patient does not have. PPI therapy would be escalated if objective gastroesophageal reflux disease was confirmed and symptom relief was inadequate with single-dose PPI. Esophageal high-resolution manometry could be considered in this setting if the patient experienced noncardiac chest pain to evaluate for an esophageal motor disorder; however, the patient does not describe chest pain or dysphagia.

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Question 34

A 46-year-old man with hypertension is referred to you for 6 months of progressively worsening chest pain that occurs after meals and with exercise. The patient denies heartburn, dysphagia, weight loss, and regurgitation. His body mass index is 31 kg/m². His chest pain did not improve with a 6-week trial of daily proton pump inhibitor (PPI).

What is the next best step in management?

- A. Ambulatory reflux monitoring with impedance testing
- B. Cardiology referral for chest pain evaluation
- C. Esophageal high-resolution manometry
- D. Escalation to double-dose PPI
- E. Upper endoscopy with biopsy

CORRECT ANSWER: B

RATIONALE

This case highlights the importance of ensuring that a cardiac source of chest pain has been ruled out before proceeding with further gastrointestinal evaluation, especially in a patient with risk factors for cardiac disease. Escalation to double-dose PPI may be considered; however, given his lack of overt symptoms of gastroesophageal reflux disease and lack of response to PPI, it is unlikely to be of benefit. If a cardiac source had been ruled out, then evaluation with upper endoscopy would be appropriate, followed by ambulatory reflux monitoring in the absence of erosive reflux findings on endoscopy. If a cardiac source had been ruled out, and upper endoscopy was normal, esophageal high-resolution manometry could be considered to assess for an esophageal motor disorder.

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Question 35

A 40-year-old woman is referred to you for evaluation of persistent heartburn and regurgitation despite optimized double-dose proton pump inhibitor (PPI) therapy and lifestyle modifications. She has lost 5 lb, and her body mass index is 21 kg/m². She has no comorbidities. She recently underwent an upper endoscopy with 96-hour wireless pH monitoring off PPI, which was consistent with nonerosive reflux disease. There was no hiatal hernia. She is interested in antireflux surgery.

Which of the following should be recommended before antireflux surgery?

- A. Additional weight loss
- B. Esophageal manometry
- C. Gastric emptying study
- D. Psychology referral
- E. Quadruple-dose PPI trial

CORRECT ANSWER: B

RATIONALE

This case highlights the importance of excluding a major esophageal motor disorder, such as achalasia, on high-resolution esophageal manometry before proceeding with antireflux surgery, as achalasia is a contraindication to antireflux surgery. Although weight management is critical to the management of gastroesophageal reflux disease, additional weight loss is unlikely to provide sufficient symptom relief for this patient, who has a normal body mass index. A gastric emptying study could be considered if gastroparesis was also suspected but is not required before referral for antireflux surgery. Psychology referral could be considered in a patient with functional heartburn and/or reflux hypersensitivity. Quadruple-dose PPI therapy has no established role.

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Question 36

A 52-year-old man with hypertension and diabetes mellitus type 2 is referred to you for 8 months of troublesome regurgitation and heartburn. He has a body mass index of 29 kg/m². He had minimal relief with single-dose proton pump inhibitor (PPI) therapy before breakfast and partial response with double-dose PPI therapy taken before breakfast and before dinner. Regurgitation after dinner and at bedtime is his most troublesome symptom.

What is the next best step in management?

- A. Counsel on weight management
- B. Increase PPI to quadruple dose
- C. Perform gastric emptying study
- D. Refer for bariatric surgery evaluation
- E. Switch PPI to before bedtime

CORRECT ANSWER: A

RATIONALE

This presentation represents typical symptoms of gastroesophageal reflux disease that are not responsive to an optimized regimen of PPI therapy. Management of refractory gastroesophageal reflux disease symptoms begins with optimizing lifestyle and weight loss. Quadruple-dose PPI therapy has no established role. A gastric emptying study would be recommended if gastroparesis was suspected. This patient does not meet criteria for bariatric surgery as his body mass index is

less than 30 kg/m². PPI therapy optimization with before-meal dosing (30-60 min before breakfast for single-dose therapy and before breakfast and dinner for double-dose therapy) would be the next step after weight management.

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Question 37

A 42-year-old man is referred to you for 3 years of troublesome regurgitation and heartburn. His heartburn responded well to single-dose proton pump inhibitor (PPI) therapy, but the regurgitation persists. On examination of his gastroesophageal junction during upper gastrointestinal endoscopy you note a gastroesophageal flap valve Hill grade 3 and a 4 cm separation between the top of the gastric folds and the crural diaphragm.

Which of the following is the best explanation for this patient's poor response to PPI therapy?

- A. Disrupted antireflux barrier
- B. Delayed gastric emptying
- C. Gastric acid hypersecretion
- D. Increased frequency of transient lower esophageal sphincter relaxations
- E. Ineffective esophageal motility

CORRECT ANSWER: A

RATIONALE

All of the choices are possible contributors to worsened reflux symptoms and poor response to

PPI. However, this presentation represents a disrupted antireflux barrier in the setting of a large hiatal hernia. Intraabdominal strain and retained bolus in the hiatal hernia are the primary drivers of gastroesophageal reflux disease (GERD) in this setting and cannot be reversed with PPI therapy. Delayed gastric emptying can worsen reflux disease and lead to regurgitation of gastric contents, but there is no reason to suspect this in this patient. Hypersecretion of gastric acid is an uncommon source of PPI-refractory GERD but is not indicated in the case presentation. Although transient lower esophageal sphincter relaxations are the general drivers of GERD, they are less often observed as a cause of reflux in the setting of a large hiatal hernia. Poor esophageal motility can lead to reduced clearance of refluxate, but this case includes no indication of poor motility (dysphagia or manometry revealing such).

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Question 38

A 37-year-old man is referred to you for 2 years of heartburn that has progressed to a daily occurrence. He denies regurgitation, chest pain, sore throat, and cough. His body mass index is 21 kg/m². His symptoms have not improved with a 12-week trial of proton pump inhibitor therapy. Upper gastrointestinal endoscopy shows normal findings without evidence of hiatal hernia, esophagitis, or stricture.

What is the next best step?

- A. Ambulatory reflux monitoring
- B. Esophageal high-resolution manometry
- C. Gastrointestinal psychology referral
- D. Low-dose antidepressant trial
- E. Nissen fundoplication

CORRECT ANSWER: A

RATIONALE

This presentation represents typical symptoms of gastrointestinal reflux disease (GERD) that are not responsive to proton pump inhibitor therapy and with no erosive findings on endoscopy. The patient has not yet been proven to have GERD. The next step is objective evaluation for nonerosive reflux disease with ambulatory reflux monitoring performed off acid suppression to assess for esophageal acid exposure time and symptom-reflux association. Esophageal high-resolution manometry is not a diagnostic tool for GERD. Gastrointestinal psychology referral and antidepressants are treatment options for patients diagnosed with functional heartburn or reflux hypersensitivity. Diagnosis of functional heartburn and reflux hypersensitivity requires ambulatory reflux monitoring. Antireflux surgery should be considered only in patients with established objective GERD.

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Question 39

A 22-year-old woman is referred to you for 8 months of progressive dysphagia to solids and liquids, as well as regurgitation, chest pain, and a 5 lb unintentional weight loss. She has no comorbidities and is not on any medications. Her symptoms have not improved with proton pump inhibitor therapy. She undergoes an upper gastrointestinal endoscopy, which shows a fluid-filled esophagus and puckering at the esophago-gastric junction. There is moderate resistance to the endoscope on passage across the esophago-gastric junction. Evaluation of the stomach and small bowel, including retroflexion at the gastric cardia, reveals normal findings. Biopsies of the distal and proximal esophagus are normal.

What is the next best step?

- A. Ambulatory reflux monitoring
- B. Chest/abdomen computed tomography
- C. Esophageal manometry
- D. Gastric emptying study
- E. Dietician referral

CORRECT ANSWER: C

RATIONALE

This presentation represents nonobstructive dysphagia with concern for an esophageal motility disorder such as achalasia, and the next step in evaluation would be high-resolution esophageal manometry. Ambulatory reflux monitoring could be considered if reflux symptoms had been present and achalasia had been excluded. Cross-sectional imaging with computed tomography can be considered if pseudoachalasia had been suspected. A gastric emptying study could be considered if gastroparesis had been suspected. Although a referral to a dietician may be part of the treatment plan, this is not the next best step.

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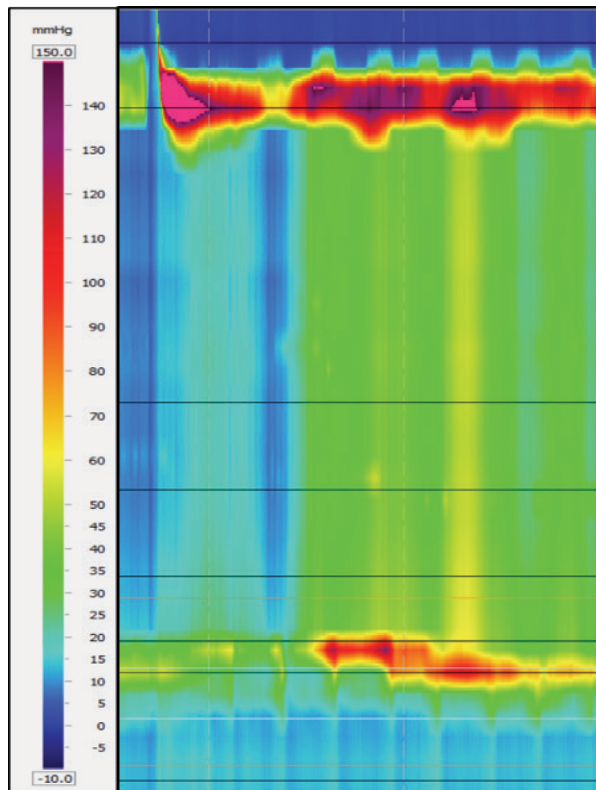
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Question 40

A 43-year-old man is referred to you for 8 months of progressive dysphagia to solids and liquids, as well as bland regurgitation, chest pain, and a 6 lb weight loss. He has no comorbidities and is not on any medications. His upper gastrointestinal endoscopy was normal other than mild resistance to the endoscope on passage across the esophagogastric junction (EGJ). He undergoes an esophageal high-resolution manometry, which reveals an elevated median integrated relaxation pressure (IRP), 100% failed peristalsis, and 30% panesophageal pressurization (representative swallow in the figure below).



What is the diagnosis?

- A. Absent contractility
- B. Achalasia type 1
- C. Achalasia type 2
- D. Achalasia type 3
- E. EGJ outflow obstruction

CORRECT ANSWER: C

RATIONALE

This case represents a manometric presentation of achalasia type 2, which is characterized by inadequate lower esophageal sphincter relaxation (elevated median IRP), 100% failed peristalsis with panesophageal pressurization in 20% or more of swallows. In absent contractility, lower esophageal sphincter relaxation is intact with 100% failed peristalsis. In achalasia type 1, the median IRP is elevated with 100% failed peristalsis but without panesophageal pressurization. In achalasia type 3, the median IRP is elevated with 20% or more of swallows with premature contraction (distal latency <4.5 seconds) and the remaining swallows failed. In EGJ outflow obstruction, the median IRP is elevated in both supine and upright positions, intrabolar pressurization is noted in at least 20% of swallows, and peristalsis does not meet criteria for achalasia.

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Question 41

A 62-year-old man is referred to you for 2 years of dysphagia to solids and liquids and spastic-like chest pain. He has had a 6 lb weight loss. He has no comorbidities and is not on any medications. He undergoes upper gastrointestinal endoscopy followed by high-resolution esophageal manometry and is diagnosed with type 3 achalasia.

What is the next best step?

- A. Endoscopic botulinum toxin injection
- B. Oxycodone trial
- C. Peroral endoscopic myotomy
- D. Pneumatic dilation
- E. Proton pump inhibitor

CORRECT ANSWER: C

RATIONALE

The recommended first-line treatment for type 3 achalasia is a myotomy across the lower esophageal sphincter with proximal extension along the spastic segment in the esophagus. This is generally achieved via peroral endoscopic myotomy. Endoscopic botulinum toxin injection can be trialed for patients who are not candidates for myotomy. Opioids can lead to esophageal dysmotility; in which case, opioid cessation is recommended. Pneumatic dilation is a treatment option for type 1 and 2 achalasia but is not recommended in type 3 achalasia as it does not address the spasticity in the distal esophagus. Proton pump inhibitor therapy may be used after achalasia treatment to reduce esophageal acid exposure, but it is not a treatment option for achalasia.

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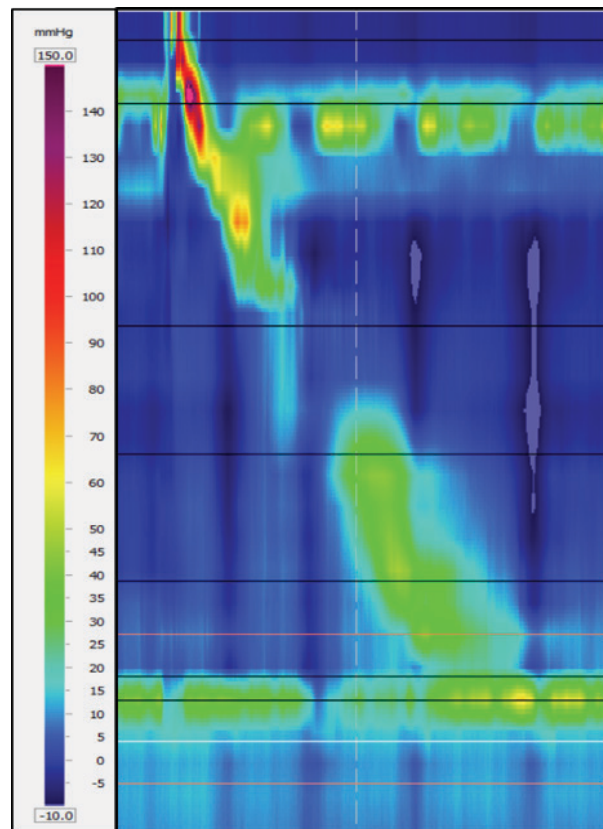
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Question 42

A 65-year-old woman with nonobstructive dysphagia to liquids undergoes an esophageal high-resolution manometry, which reveals a 1.5 cm hiatal hernia, normal median integrated relaxation pressure (IRP), 80% swallows with weak peristalsis, and 20% swallows with intact peristalsis (representative swallow in the figure below).



What is the diagnosis?

- A. Absent contractility
- B. Achalasia type 1
- C. Esophagogastric junction outflow obstruction
- D. Ineffective esophageal motility
- E. Normal esophageal motor function

CORRECT ANSWER: D

RATIONALE

This presentation represents a manometric diagnosis of ineffective esophageal motility, which is characterized by intact lower esophageal sphincter re-

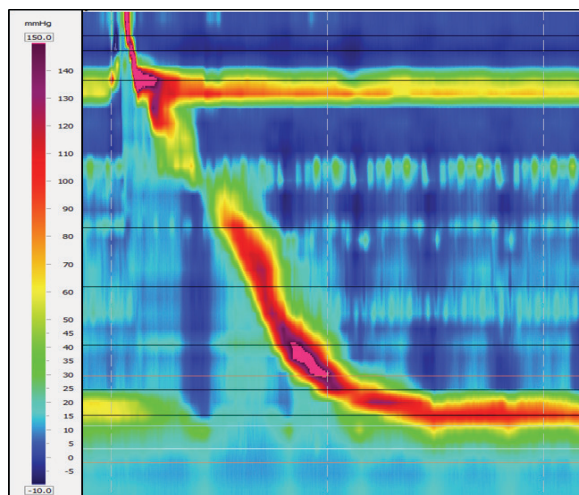
laxation (normal median IRP) with more than 70% of swallows ineffective or at least 50% swallows failed. An ineffective swallow is defined as having a distal contractile integral less than 450 mmHg-s-cm or a fragmented swallow with a peristaltic break greater than 5 cm. A failed swallow has a distal contractile integral less than 100 mmHg-s-cm. In absent contractility, lower esophageal sphincter relaxation is intact with 100% failed peristalsis. In achalasia type 1, the median IRP is elevated with 100% failed peristalsis. In esophagogastric junction outflow obstruction, the median IRP is elevated in both supine and upright positions, intrabolus pressurization is noted in at least 20% of swallows, and peristalsis does not meet criteria for achalasia.

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Question 43

A 48-year-old man with nonobstructive dysphagia to liquids and solids undergoes an esophageal high-resolution manometry, which reveals a normal median integrated relaxation pressure (IRP), 20% swallows with weak peristalsis, and 80% swallows with intact peristalsis (representative swallow in the figure below).



What is the diagnosis?

- A. Absent contractility
- B. Achalasia type 1
- C. Esophagogastric junction outflow obstruction
- D. Ineffective esophageal motility
- E. Normal esophageal motor function

CORRECT ANSWER: E

RATIONALE

This image represents a normal manometry study, showing no disorder of esophagogastric junction outflow as lower esophageal sphincter (relaxation is intact (normal median IRP) and no disorder of esophageal peristalsis. In absent contractility, lower esophageal sphincter relaxation is intact with 100% failed peristalsis. In achalasia type 1, the median IRP is elevated with 100% failed peristalsis. In esophagogastric junction outflow obstruction, the median IRP is elevated in both supine and upright positions, intrabolus pressurization is noted in at least 20% of swallows, and peristalsis does not meet criteria for achalasia. In ineffective esophageal motility, the median IRP is normal with more than 70% of swallows ineffective or at least 50% of swallows failed. An ineffective swallow is defined as having a distal contractile integral less than 450 mmHg-s-cm or a fragmented swallow with a peristaltic break greater than 5 cm. A failed swallow has a distal contractile integral less than 100 mmHg-s-cm.

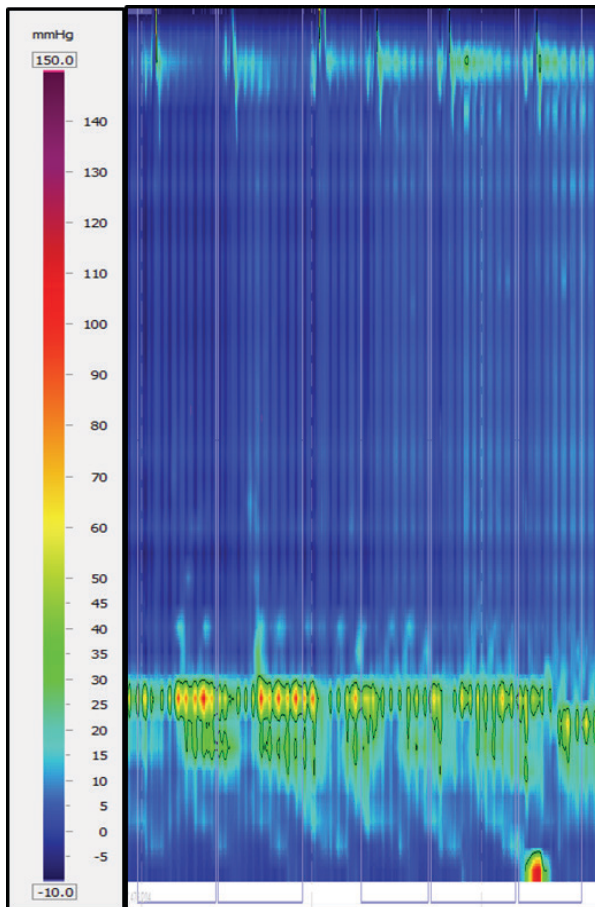
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Question 44

A 62-year-old woman undergoes high-resolution esophageal manometry for solid and liquid dysphagia after an upper gastrointestinal endoscopy was unrevealing for a mechanical source of

dysphagia and biopsies were negative for esophageal eosinophilia. Esophageal high-resolution manometry reveals a normal median integrated relaxation pressure (IRP) at the upper limit of normal and 100% failed peristalsis (representative swallow in the figure below).



What is the next step?

- A. Double-dose proton pump inhibitor trial
- B. Endoscopic botulinum toxin injection at lower esophageal sphincter
- C. Reassurance that patient does not have achalasia
- D. Surgical myotomy of lower esophageal sphincter
- E. Timed barium esophagram

CORRECT ANSWER: E

RATIONALE

This represents a case of absent contractility on manometry with inconclusive data for achalasia given the IRP at the upper limit of normal; therefore, further testing is recommended to assess lower esophageal sphincter function and exclude achalasia. Testing includes a timed barium esophagram and/or functional lumen imaging planimetry. Proton pump inhibitor therapy is not indicated, given the absence of erosive reflux findings and absence of typical reflux symptoms. Although botulinum toxin injection is a possible treatment for achalasia in patients who are not surgical or dilation candidates, the diagnosis of achalasia has not been definitively made and thus this would be an inappropriate option at this point. Based on the case presentation, achalasia has not been ruled out, and it would not be appropriate to reassure the patient that she does not have achalasia. Additionally, because achalasia has not been confirmed, surgical myotomy would not be indicated at this time.

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Question 45

A 55-year-old man is referred to you for a recent diagnosis of achalasia. He began experiencing dysphagia to solids and liquids 7 months ago along with bland regurgitation and chest spasm. He has not lost weight. He underwent an upper gastrointestinal endoscopy that was concerning for achalasia and subsequently underwent a high-resolution esophageal manometry that confirmed

a diagnosis of type 1 achalasia. He has no past medical history, is not on any medications, and has not undergone any treatment for achalasia.

What is the best management recommendation?

- A. Calcium channel blocker trial
- B. Endoscopic balloon dilation to 20 mm
- C. Endoscopic botulinum toxin injection
- D. Percutaneous endoscopic gastrostomy tube placement
- E. Surgical or endoscopic myotomy referral

CORRECT ANSWER: E

RATIONALE

This presentation represents a patient with type 1 achalasia who is a candidate for first-line therapy. First-line therapy for achalasia includes peroral endoscopic myotomy, laparoscopic Heller myotomy, or pneumatic dilation to 30 mm or greater. Pharmacologic management with botulinum toxin injection or calcium channel blockers are second-line therapy options for patients who are not candidates for first-line therapy. A traditional through-the-scope balloon dilation to 20 mm does not sufficiently address the lower esophageal sphincter and is not recommended in the treatment of achalasia. Percutaneous endoscopic gastrostomy tube placement is rarely recommended in achalasia when patients are unable to tolerate oral nutrition.

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Question 46

A 23-year-old woman is referred to you for chronic regurgitation and vomiting, typically after meals. She has a past medical history of bulimia and is enrolled in an eating disorders program. Her last purging episode was over a year ago. She denies chest pain, heartburn, or dysphagia. She has had a 4 lb weight loss over the past year. Her symptoms have not improved with proton pump inhibitor therapy.

What is the most likely diagnosis?

- A. Absent contractility
- B. Achalasia type 1
- C. Distal esophageal spasm
- D. Gastroesophageal reflux disease
- E. Rumination syndrome

CORRECT ANSWER: E

RATIONALE

This presentation represents a patient who likely has rumination syndrome, a behavioral disorder in which food is regurgitated through active contraction of the abdomen and is rechewed, reswallowed, or spit out. Rumination syndrome is more common in patients with a history of bulimia and can often masquerade as gastroesophageal reflux disease (GERD). However, in GERD, the reflux of gastric contents is not due to voluntary active abdominal contraction, and symptoms of GERD often include nociceptive responses to acidic refluxate, such as heartburn or chest pain. Absent contractility, an esophageal motility disorder characterized by failed esophageal peristalsis, may present with dysphagia and/or reflux symptoms. Achalasia, an esophageal motility disorder of impaired lower esophageal sphincter relaxation

and esophageal peristalsis, typically presents with dysphagia, regurgitation, and weight loss. Distal esophageal spasm, an esophageal motility disorder of spastic contractions, typically presents with dysphagia and/or noncardiac chest pain.

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Question 47

A 42-year-old man is referred to you for dysphagia to liquids for the past 6 months that has progressively worsened to occurring with every meal. He has a past medical history of asthma. He denies heartburn, regurgitation, and chest pain. His weight has been stable. On upper gastrointestinal endoscopy, his esophagus appears normal. Biopsies of the proximal and distal esophagus are also normal. On high-resolution esophageal manometry, median integrated relaxation pressure (IRP) is normal and 100% of peristalsis is intact.

What is the most likely diagnosis?

- A. Absent contractility
- B. Achalasia type 1
- C. Distal esophageal spasm
- D. Eosinophilic esophagitis
- E. Functional dysphagia

CORRECT ANSWER: E

RATIONALE

This presentation represents a case of functional dysphagia, defined by Rome IV as chronic, troublesome dysphagia in the absence of esophageal structural abnormalities, mucosal abnormalities, gastroesophageal reflux disease, eosinophilic esophagitis, or major esophageal motor disorder. On high-resolution esophageal manometry, absent contractility presents with normal median IRP and

100% failed peristalsis; achalasia type 1, with elevated median IRP and 100% failed peristalsis; and distal esophageal spasm, with normal median IRP and at least 20% peristalsis with premature contraction. Eosinophilic esophagitis is diagnosed by the presence of elevated eosinophils on high-power field of esophageal biopsies and often in the context of mucosal abnormalities detected on endoscopy.

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Question 48

A 67-year-old man is referred to you for dysphagia to solids and liquids for 2 years. Approximately 3 years ago, he was in a motor vehicle accident and developed chronic back pain for which he takes oxycodone 3 times daily. He also experiences postprandial chest pain. His body mass index is 29 kg/m², and he has lost 5 lb over the past year. On upper gastrointestinal endoscopy, the esophagus is normal in appearance. Biopsies of the proximal and distal esophagus are normal. His high-resolution esophageal manometry is abnormal with 60% of swallows premature in the setting of a normal median integrated relaxation pressure, suggestive of distal esophageal spasm.

What is the next best step in management?

- A. Balloon dilation
- B. Endoscopic myotomy
- C. Opioid cessation
- D. Proton pump inhibitor
- E. Weight loss

CORRECT ANSWER: C

RATIONALE

This presentation represents opioid-induced esophageal dysmotility with a distal esophageal

spasm pattern; thus, the first recommendation should be opioid cessation. Balloon dilation is not a treatment option for distal esophageal spasm. Surgical or endoscopic myotomy can be considered for distal esophageal spasm if patients have not responded to lifestyle and medical management. When distal esophageal spasm is present in the setting of gastroesophageal reflux disease, a trial of proton pump inhibitor therapy is recommended along with weight loss in patients who are overweight or obese.

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Yadlapati R, Kahrilas PJ, Fox MR, et al. Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0®. *Neurogastroenterol Motil.* 2021;33(1):e14058. doi:10.1111/nmo.14058

Chen JW, Savarino E, Smout A, et al. Chicago Classification Update (v4.0): Technical review on diagnostic criteria for hypercontractile esophagus. *Neurogastroenterol Motil.* 2021;33(6):e14115. doi:10.1111/nmo.14115

Question 49

An 87-year-old woman is referred to you for 3 months of rapidly progressive dysphagia to solids and liquids and a 15 lb unintentional weight loss. On barium esophagram, her esophagus appears dilated with birds-beaking at the gastroesophageal junction and contrast retention. She undergoes an upper gastrointestinal endoscopy, which shows a fluid-filled esophagus and puckering at the esophagogastric junction (EGJ). There is moderate resistance to the endoscope on passage across the EGJ. On retroflexion, extensive ulceration is noted at the gastric cardia.

What condition should you be most concerned about?

- A. Achalasia type I
- B. EGJ outflow obstruction
- C. Gastric intestinal metaplasia

- D. Gastric outlet obstruction
- E. Pseudoachalasia

CORRECT ANSWER: E

RATIONALE

This represents a case concerning for pseudoachalasia. Pseudoachalasia describes an obstructive process at the EGJ, classically a tumor, that clinically presents with symptoms and findings similar to achalasia and often with rapid onset of symptoms and weight loss. Although the esophagram findings are classic for achalasia, the endoscopic finding of extensive ulceration at the cardia is more concerning for an infiltrative process such as malignancy causing pseudoachalasia. EGJ outflow obstruction is a manometric diagnosis, which is made when the median IRP is elevated in both supine and upright positions, intrabolar pressurization is noted in at least 20% of swallows, and peristalsis does not meet criteria for achalasia because some peristalsis is preserved. Gastric intestinal metaplasia is a histologic diagnosis characterized by precancerous changes of the gastric mucosa with intestinal epithelium. Gastric outlet obstruction is due to mechanical obstruction in proximity to the pyloric outlet and does not affect the esophagus.

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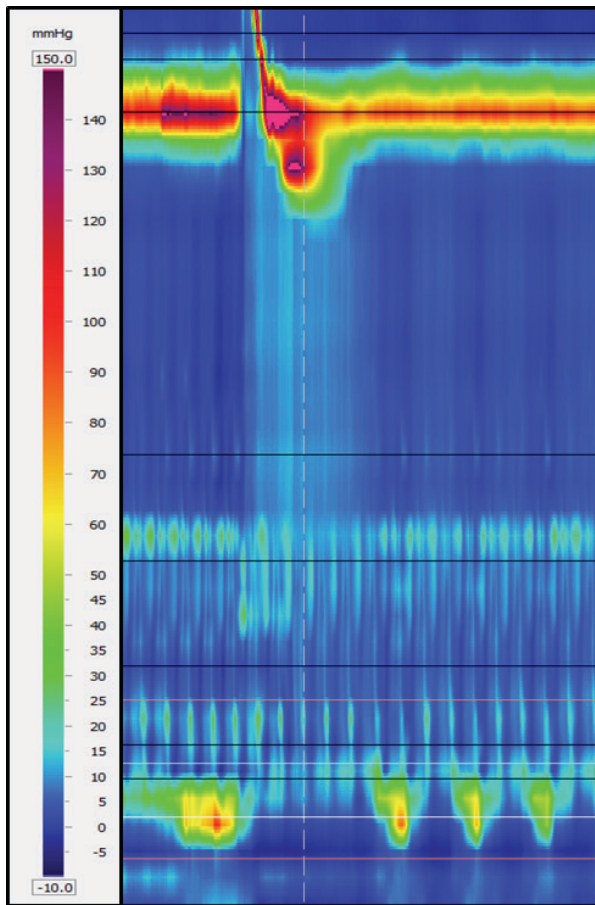
Gyawali CP, Carlson DA, Chen JW, Patel A, Wong RJ, Yadlapati RH. ACG Clinical Guidelines: Clinical Use of Esophageal Physiologic Testing. *Am J Gastroenterol.* 2020;115(9):1412-1428. doi:10.14309/ajg.0000000000000734

Vaezi MF, Pandolfino JE, Yadlapati RH, Greer KB, Kavitt RT. ACG Clinical Guidelines: Diagnosis and Management of Achalasia. *Am J Gastroenterol.* 2020;115(9):1393-1411. doi:10.14309/ajg.0000000000000731

Question 50

A 34-year-old woman is referred to you for dysphagia to solids and liquids with mild regurgitation and heartburn. She has a history of depres-

sion and Raynaud's phenomenon. She describes several years of joint aches. On upper gastrointestinal endoscopy, her esophageal examination is normal, and the esophagogastric junction is wide open and easily traversed. A representative swallow from her high-resolution esophageal manometry is below.



contractility on esophageal manometry along with Raynaud's phenomenon and joint pains, raises suspicion for a mixed connective tissue disorder such as scleroderma/systemic sclerosis. Systemic sclerosis can result in gastrointestinal dysmotility and, in the esophagus, can impact the smooth muscles and manifest as absent contractility. The other answer choices are not associated with absent contractility. Bipolar disorder is not known to impact esophageal motility. Chagas disease has been associated with achalasia. Dermatomyositis affects the skeletal muscle and can lead to oropharyngeal dysphagia or proximal esophageal dysmotility. Parkinson's disease can also lead to an oropharyngeal dysphagia.

REFERENCE

Yadlapati R, Kahrilas PJ, Fox MR, et al. Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0[®]. *Neurogastroenterol Motil.* 2021;33(1):e14058. doi:10.1111/nmo.14058

What comorbidity is most likely to be present in this patient?

- A. Bipolar disorder
- B. Chagas disease
- C. Dermatomyositis
- D. Parkinson's disease
- E. Systemic sclerosis

CORRECT ANSWER: E

RATIONALE

This case, representing a patient with absent

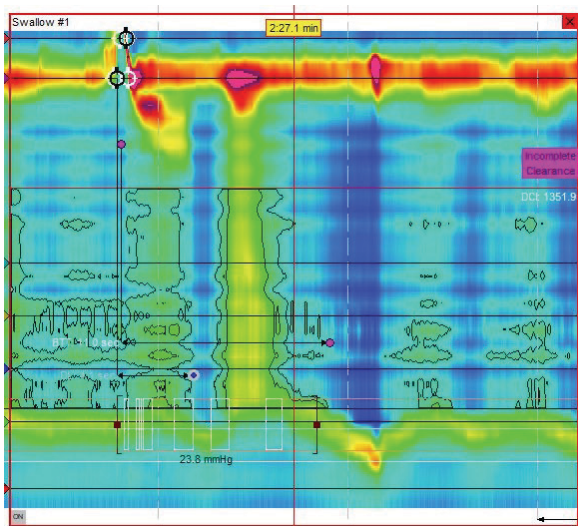
CHAPTER 10

Neurogastroenterology and Gastrointestinal motility

Nitin Ahuja, MD and Ami Patel, MD

Question 1

A 40-year-old woman presents to clinic with a chief complaint of refractory heartburn over the past 6 months. Serial trials of high-dose pantoprazole and omeprazole have been unsuccessful. She experienced self-limited dyspepsia 1 year ago for which she underwent an upper endoscopy, the results of which were normal. On further questioning, she endorses occasional postprandial regurgitation and 10-pound weight loss. A high-resolution esophageal manometry is performed, with a representative supine swallow reproduced below.



Which of the following is the most likely diagnosis?

- A. Esophagogastric junction outflow obstruction
- B. Ineffective esophageal motility
- C. Type 1 achalasia

- D. Type 2 achalasia
- E. Hypercontractile (jackhammer) esophagus

CORRECT ANSWER: D

RATIONALE

Refractory heartburn is a common clinical scenario leading to an eventual diagnosis of achalasia, which is a major disorder of esophageal motility. Type 2 achalasia is characterized on esophageal manometry by impaired deglutitive relaxation of the lower esophageal sphincter accompanied by consistent failure of peristalsis with at least 20% of swallows demonstrating a pattern of panesophageal pressurization, as is shown in this image.

REFERENCE

Yadlapati R, Kahrilas PJ, Fox MR, et al. Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0[®]. *Neurogastroenterol Motil.* 2021;33(1):e14058. doi:10.1111/nmo.14058

Question 2

A 50-year-old woman presents to clinic with a complaint of persistent heartburn. Once-daily omeprazole has been incompletely helpful. A review of systems is notable for Raynaud's phenomenon, bilateral joint stiffness, and intermittent postprandial abdominal bloating. Serologies recently ordered by her primary physician were notable for positive anti-nuclear antibody and anti-topoisomerase I antibody titers. If an

esophageal manometry were performed, what would be the most likely pattern identified?

- A. Esophagogastric junction outflow obstruction
- B. Type 1 achalasia
- C. Type 2 achalasia
- D. Type 3 achalasia
- E. Absent contractility

CORRECT ANSWER: E

RATIONALE

The patient's likely diagnosis is systemic sclerosis (scleroderma), as signaled by her comorbid symptoms and positive autoimmune serologies. Ninety percent of patients with this condition will have esophageal involvement, with the classic manometric pattern being absent contractility, characterized by consistently failed (absent) peristalsis with hypotonicity of the lower esophageal sphincter. The association is common enough that "scleroderma esophagus" is sometimes used as a synonym for absent contractility. In a prospective series of 200 patients with systemic sclerosis undergoing esophageal manometry, absent contractility was the most commonly seen pattern (56%), followed by normal motility (26%), and ineffective esophageal motility (10%).

REFERENCE

Crowell MD, Umar SB, Griffing WL, DiBaise JK, Lacy BE, Vela MF. Esophageal Motor Abnormalities in Patients With Scleroderma: Heterogeneity, Risk Factors, and Effects on Quality of Life. *Clin Gastroenterol Hepatol*. 2017;15(2):207-213.e1. doi:10.1016/j.cgh.2016.08.034

Question 3

A 55-year-old man presents to clinic with intermittent difficulty swallowing for the past month. His past medical history is notable for insulin-dependent diabetes, coronary artery disease treated with dual antiplatelet therapy, and a resolving occupational injury for which he takes oxycodone once or twice daily. An upper endoscopy and

barium esophagram are unrevealing. A 4-week trial of omeprazole is unhelpful. An esophageal manometry reveals esophagogastric junction outflow obstruction (EGJOO).

What is the next most appropriate step?

- A. Hydrostatic balloon dilation of the lower esophageal sphincter
- B. Pneumatic balloon dilation of the lower esophageal sphincter
- C. Botulinum toxin injection to the lower esophageal sphincter
- D. Heller myotomy with partial fundoplication
- E. Opioid discontinuation followed by repeat esophageal manometry

CORRECT ANSWER: E

RATIONALE

Opioid-induced esophageal dysfunction refers to an alteration in esophageal motility mediated by exogenous opioids. Manometric results vary, but EGJOO is among the most common patterns noted. Optimal management for EGJOO and opioid-induced esophageal dysfunction have yet to be clarified, but as a first step, among patients on short-term opioid therapy that can reasonably be held for at least 24 hours, manometry should ideally be performed off opioid therapy to distinguish between the 2 entities.

REFERENCE

Ratuapli SK, Crowell MD, DiBaise JK, et al. Opioid-Induced Esophageal Dysfunction (OIED) in Patients on Chronic Opioids. *Am J Gastroenterol*. 2015;110(7):979-984. doi:10.1038/ajg.2015.154

Question 4

A 68-year-old woman with a few months history of muscle weakness is seen for dysphagia to both solids and liquids that occurs immediately after swallowing. The patient reports coughing and choking during meals with occasional nasal

regurgitation. An upper endoscopy is normal. An esophageal manometry reveals normal peristalsis throughout the esophagus. The lower esophageal sphincter basal pressure and function were all within the normal range. The upper esophageal sphincter basal pressure was low normal, and the amplitudes in the pharynx and proximal esophagus were abnormally low.

What is the likely diagnosis?

- A. Systemic sclerosis
- B. Ineffective motility disorder
- C. Achalasia
- D. Polymyositis
- E. Systemic lupus erythematosus

CORRECT ANSWER: D

RATIONALE

The history of coughing and choking and nasal regurgitation are classic signs of oropharyngeal dysphagia due to altered function of the proximal striated muscles of the upper esophagus and pharynx. Therefore, achalasia and ineffective motility disorder of the esophagus are incorrect, as these would cause esophageal dysphagia. Systemic sclerosis solely affects the distal two-thirds of smooth muscle of the esophagus and often presents with peptic strictures due to significant reflux through the incompetent lower esophageal sphincter. Polymyositis affects swallowing by involving the striated muscle of the pharynx and esophagus in up to 50% to 70% of these patients. Systemic lupus erythematosus may result in nonspecific motor abnormalities of the esophagus.

REFERENCE

Gasiorowska A et al. Current approach to dysphagia *Gastroenterol Hepatol* 2009;5:269-79.

Sheehan NJ. Dysphagia and other manifestations of oesophageal involvement in the musculoskeletal diseases, *Rheumatology*, Volume 47, Issue 6, June 2008, Pages 746–752, <https://doi.org/10.1093/rheumatology/ken029>

Question 5

A 20-year-old woman presents to clinic with a history of nausea, vomiting, and early satiety after an episode of food poisoning 6 months ago. She has no significant past medical or surgical history, and she takes no medications. She has lost 5 pounds over this interval, and her current body mass index is 22 kg/m². An upper endoscopy is unrevealing. A gastric scintigraphy reveals 31% meal retention at 4 hours (normal <10%).

Which of the following dietary recommendations is most appropriate?

- A. Restriction of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols
- B. Low-fat, low-fiber diet
- C. Enteral feeding via nasogastric tube
- D. Enteral feeding via percutaneous gastrostomy tube
- E. Total parenteral nutrition

CORRECT ANSWER: B

RATIONALE

This patient meets diagnostic criteria for gastroparesis (most likely post-infectious in etiology). Typical dietary recommendations for patients with gastroparesis include avoidance of fat (especially in solid food) and fiber, as both are associated with increased symptoms, perhaps by virtue of a tendency toward further gastric retention. Additional guidance might include favoring liquid over solid nutrition when symptoms are severe and/or adherence to a small particle size diet, selecting for foods that can be easily reduced to a soft consistency. Nutritional supplementation may be considered in the setting of severe or uncontrolled weight loss due to symptoms refractory to medical intervention, which is not the case here. When nutritional supplementation is under consideration, enteral nutrition is generally favored over parenteral nutrition given their respective risk profiles.

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Homko CJ, Duffy F, Friedenberg FK, Boden G,

Parkman HP. Effect of dietary fat and food consistency on gastroparesis symptoms in patients with gastroparesis. *Neurogastroenterol Motil.* 2015;27(4):501-508. doi:10.1111/nmo.12519

Olausson EA, Störsrud S, Grundin H, Isaksson M, Attvall S, Simrén M. A small particle size diet reduces upper gastrointestinal symptoms in patients with diabetic gastroparesis: a randomized controlled trial. *Am J Gastroenterol.* 2014;109(3):375-385. doi:10.1038/ajg.2013.453

Question 6

A 45-year-old woman presents to clinic with a history of refractory heartburn despite treatment with omeprazole 40 mg twice daily before meals. She reports having gained 5 pounds over the past 5 years, and her current body mass index is 30 kg/m². An upper endoscopy demonstrates a medium-sized hiatal hernia. A pH/impedance study performed on therapy demonstrates an esophageal acid exposure time of 8.4%. An esophageal manometry yields a diagnosis of ineffective esophageal motility. On the manometry tracing, a rapid sequence of 5 additional swallows leads to an augmented final peristaltic contraction. She is subsequently referred to a surgeon to discuss antireflux surgery.

Which of the following is true about this patient?

- A. She has intact peristaltic reserve, which reduces the likelihood of post-fundoplication dysphagia
- B. She has intact peristaltic reserve, which increases the likelihood of post-fundoplication dysphagia
- C. She lacks peristaltic reserve, which reduces the likelihood of post-fundoplication dysphagia
- D. She lacks peristaltic reserve, which increases the likelihood of post-fundoplication dysphagia
- E. She should undergo a Roux-en-Y gastric bypass instead of fundoplication

CORRECT ANSWER: A

RATIONALE

The maneuver described at the end of the manometry recording, termed a multiple rapid swallow sequence, is intended to assess for peristaltic reserve, which is demonstrated by an augmented final peristaltic contraction (ie, greater in vigor than the average of the preceding 10 swallows). Intact peristaltic reserve, even in the context of a manometric diagnosis of ineffective esophageal motility, has been associated with reduced likelihood of dysphagia after fundoplication. Roux-en-Y gastric bypass can be an effective antireflux surgery but is generally reserved for obese patients with a body mass index greater than 35 kg/m².

REFERENCE

Gyawali CP, Sifrim D, Carlson DA, et al. Ineffective esophageal motility: Concepts, future directions, and conclusions from the Stanford 2018 symposium. *Neurogastroenterol Motil.* 2019;31(9):e13584. doi:10.1111/nmo.13584

Question 7

A 43-year-old man presents with progressive dysphagia and weight loss over the past 2 years. He had an endoscopy that revealed a dilated esophagus and mild resistance through the lower esophageal sphincter, which appeared normal. There was no stricture or mass. Barium esophagram is shown below:



Which of the following manometric findings would you expect to find in this patient?

- A. Decreased distal latency (2.5 seconds) in 50% of swallows with a normal integrated residual pressure (IRP)
- B. Elevated IRP with normal distal latency and distal contractile index (DCI)
- C. Elevated IRP with pan-esophageal pressurization
- D. Eighty percent of swallows with DCI between 200-300 mmHg-s-cm

CORRECT ANSWER: C

RATIONALE

The esophagram of this patient presenting with dysphagia revealed a dilated esophagus with “bird’s beak” tapering at the lower esophageal sphincter, which is classic for achalasia. Increased IRP with panesophageal pressurization (answer C) is the characteristic finding of type II achalasia. A normal IRP with decreased distal latency in more than 20% of swallows represents distal esophageal spasm, which may reveal a “corkscrew esophagus” on esophagram (answer A). An elevated IRP with normal DCI and distal latency (answer B) indicates esophagogastric junction outflow obstruction (EGJOO). An increase in weak swallows (DCI between 100 to 450 mmHg-s-cm) would suggest ineffective esophageal motility (answer D).

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Question 8

A 35-year-old woman presents to clinic with a chief complaint of borborygmi. She has a past medical history of obesity treated with a Roux-en-Y gastrojejunostomy 1 year ago, which has led to weight loss of 33 pounds. On review of systems, she also endorses early satiety and intermittent postprandial sweating and lightheadedness. She wonders if the borborygmi might indicate a dietary intolerance.

Which of the following is the most appropriate dietary recommendation?

- A. Preferential ingestion of simple over complex carbohydrates
- B. Empiric trial of a gluten-free diet
- C. Liberal fluid intake during meals
- D. Avoidance of reclining for 2 to 3 hours after meals
- E. Multiple small meals daily

CORRECT ANSWER: E

RATIONALE

Based on her clinical presentation, this patient likely has dumping syndrome after bariatric surgery. Dumping syndrome is related to rapid transit of gastric contents into the small intestine. Dietary recommendations that might benefit the patient in these circumstances aim to minimize large nutrient loads to the small intestine and include multiple (at least 4 to 6) small meals daily, reducing total carbohydrate ingestion in favor of fats and proteins, favoring complex over simple (ie, easily absorbed) carbohydrates, staying upright for 30 minutes immediately after meals, and separating the ingestion of solids and liquids by at least 30 minutes.

REFERENCE

Scarpellini E, Arts J, Karamanolis G, et al. International consensus on the diagnosis and management of dumping syndrome. *Nat Rev Endocrinol*. 2020;16(8):448-466. doi:10.1038/s41574-020-0357-5

Question 9

An 80-year-old man presents to the clinic with a 6-month history of difficulty swallowing. He denies coughing, substernal chest pain, or pain with swallowing. His partner notes that he seems to have lost a bit of weight over the past few months, and that his breath has become progressively foul-smelling. An upper endoscopy with random biopsies of the esophagus is unremarkable apart from mild difficulty traversing the upper esophageal sphincter.

What is the next most appropriate step?

- A. Esophageal manometry
- B. pH/impedance testing
- C. Empiric therapy with a daily proton pump inhibitor
- D. Barium swallow study
- E. Cross-sectional imaging of the chest

CORRECT ANSWER: D

RATIONALE

This patient likely has a Zenker diverticulum resulting from cricopharyngeal dysfunction. This diagnosis is most often noted in the seventh and eighth decades of life and, of the listed options, would be best confirmed with barium radiography. Empiric treatment with a proton pump inhibitor and pH/impedance testing suggest gastroesophageal reflux disease, which is a less likely explanation for dysphagia in the absence of typical heartburn symptoms. Esophageal dysmotility or intrathoracic malignancy, as would be assessed by manometry or cross-sectional imaging, are worth excluding but still less likely in this case given the associated halitosis and endoscopic suspicion of distorted cricopharyngeal anatomy.

REFERENCE

Law R, Katzka DA, Baron TH. Zenker's Diverticulum. *Clin Gastroenterol Hepatol*. 2014;12(11):1773-e112. doi:10.1016/j.cgh.2013.09.016

Question 10

A 30-year-old woman with no significant past medical history presents to clinic with 3 months of progressive dysphagia, regurgitation, and an 11-pound weight loss. She undergoes an upper endoscopy that demonstrates fluid stasis in the distal esophagus with resistance traversing the lower esophageal sphincter, although there is no stricture or mass. A barium esophagram demonstrates dilation of the esophageal body with smooth tapering toward the lower esophageal sphincter. Her manometry demonstrates 100% of failed swallows with no discernible contractile activity in the esophageal body and reliably incomplete relaxation of the lower esophageal sphincter. She returns to clinic to discuss therapeutic options.

Which of the following statements is correct?

- A. Pneumatic dilation is more effective than Heller myotomy for patients with this achalasia subtype
- B. Hydrostatic dilation is more effective than pneumatic dilation for patients with this achalasia subtype
- C. She has an increased risk of esophageal cancer that will not be eliminated by definitive sphincter-disrupting therapy
- D. Definitive sphincter-disrupting therapy should only be offered after a successful response to a trial of botulinum toxin injection
- E. Definitive sphincter-disrupting therapy should only be offered after cross-sectional imaging of the chest to exclude malignancy

CORRECT ANSWER: C

RATIONALE

This patient has been diagnosed with type 1 achalasia. Patients with primary achalasia of any subtype have an increased risk of esophageal squamous cell carcinoma that persists even after sphincter-disrupting therapy, no matter the modality chosen. Despite this, routine endoscopic surveillance has not shown benefit in research to date. Type 1 achalasia responds equally well

to pneumatic dilation and Heller myotomy. Hydrostatic dilation is not useful in the treatment of achalasia. Botulinum toxin injection as a treatment for achalasia is generally reserved for patients whose medical comorbidities preclude more definitive therapeutic options. Pseudoachalasia secondary to neoplasm should be considered under appropriate clinical circumstances, but suspicion of an underlying malignancy is low in this young and otherwise healthy patient.

REFERENCES

Rohof WO, Salvador R, Annese V, et al. Outcomes of treatment for achalasia depend on manometric subtype. *Gastroenterology*. 2013;144(4):718-e14. doi:10.1053/j.gastro.2012.12.027

Vaezi MF, Pandolfino JE, Yadlapati RH, Greer KB, Kavitt RT. ACG Clinical Guidelines: Diagnosis and Management of Achalasia. *Am J Gastroenterol*. 2020;115(9):1393-1411. doi:10.14309/ajg.0000000000000731

Question 11

Patients with achalasia who undergo technically successful per-oral endoscopic myotomy (POEM) are at increased risk of which of the following?

- A. Cricopharyngeal bar
- B. Erosive esophagitis
- C. *Helicobacter pylori* gastritis
- D. Peptic ulcer disease
- E. Gastroparesis

CORRECT ANSWER: B

RATIONALE

POEM has demonstrated efficacy rates similar to Heller myotomy and in some cases superior to pneumatic dilation for the treatment of achalasia. In contrast to Heller myotomy, which is usually performed contemporaneously with a fundoplication, POEM is not accompanied by an antireflux procedure. Disruption of the lower esophageal sphincter leads to an increased risk

of gastroesophageal reflux disease and its associated complications, including erosive esophagitis, peptic strictures, and de novo Barrett's esophagus, particularly among patients who are not using acid-suppressive medications. The other listed options have not been associated with the performance of POEM.

REFERENCES

Modayil RJ, Zhang X, Rothberg B, et al. Peroral endoscopic myotomy: 10-year outcomes from a large, single-center U.S. series with high follow-up completion and comprehensive analysis of long-term efficacy, safety, objective GERD, and endoscopic functional luminal assessment. *Gastrointest Endosc*. 2021;94(5):930-942. doi:10.1016/j.gie.2021.05.014

Ponds FA, Fockens P, Lei A, et al. Effect of Peroral Endoscopic Myotomy vs Pneumatic Dilation on Symptom Severity and Treatment Outcomes Among Treatment-Naive Patients With Achalasia: A Randomized Clinical Trial. *JAMA*. 2019;322(2):134-144. doi:10.1001/jama.2019.8859

Question 12

A 25-year-old man arrives at the emergency department with refractory vomiting. It is his third presentation for the same complaint in the past 3 months, though he reports that he has suffered through similar episodes at home intermittently for the past year. He states that his symptoms usually resolve after 12 to 24 hours with intravenous fluids, ondansetron, and diphenhydramine. Between episodes, he feels completely well. He has no significant past medical history apart from longstanding insomnia, for which he self-medicates with nightly cannabis.

Which of the following is the next best step?

- A. Counsel regarding cannabis cessation
- B. Twice-daily therapy with a proton pump inhibitor

- C. Order a 4-hour solid-phase gastric scintigraphy
- D. Obtain an abdominal radiograph to exclude obstruction
- E. Order urine porphobilinogen and urine aminolevulinic acid

CORRECT ANSWER: A

RATIONALE

This patient's presentation is most consistent with cannabinoid hyperemesis syndrome (CHS). As defined by Rome IV criteria, CHS is phenotypically similar to cyclic vomiting syndrome but occurs in the context of regular (usually daily) cannabis use. Symptoms are typified by episodic refractory vomiting punctuated by symptom-free intervals. CHS is a clinical diagnosis. The first step in management is cannabis cessation, the necessary duration of which is not well established, though many experts recommend at least 6 months. The other listed options query clinical entities (gastroesophageal reflux disease (answer B), gastroparesis (answer C), intestinal obstruction (answer D), acute intermittent porphyria (answer E) that are possible but much less likely explanations of this patient's presentation.

REFERENCES

Venkatesan T, Levinthal DJ, Li BUK, et al. Role of chronic cannabis use: Cyclic vomiting syndrome vs cannabinoid hyperemesis syndrome. *Neurogastroenterol Motil.* 2019;31 Suppl 2(Suppl 2):e13606. doi:10.1111/nmo.13606

Question 13

A 50-year-old woman is admitted to the intensive care unit after presenting with tachycardia and hypotension following multiple episodes of hematemesis. Her past medical history is only notable for chronic joint pain for which she takes ibuprofen as needed. She is hemodynamically stabilized with intravenous fluids and given a pantoprazole infusion. An urgent bedside endoscopy reveals a normal esophagus; a small volume of old

blood in the duodenum; and a large volume of old blood mixed with clot in the stomach that precludes complete visualization of the gastric mucosa. Which of the following medications might be considered as a next step based on these findings?

- A. Intravenous ceftriaxone
- B. Intravenous erythromycin
- C. Intravenous famotidine
- D. Oral sucralfate
- E. Oral rifaximin

CORRECT ANSWER: B

RATIONALE

Erythromycin is a macrolide antibiotic that also has prokinetic effects in the foregut, via motilin-like effect on gastric musculature by binding to smooth muscle receptors and myoenteric neurons, which can facilitate clearance of gastric contents in advance of a repeat upper endoscopy. It has been shown to decrease need for repeat endoscopy for bleeding. It may also be used for treatment of gastroparesis but is not as effective as metoclopramide. Other listed options have no role in this case: there is no mention of underlying liver dysfunction to support the use of ceftriaxone or rifaximin, and there is no value to famotidine or sucralfate as an adjunct to continuous proton pump inhibitor therapy.

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Barkun AN, Bardou M, Martel M, Gralnek IM, Sung JJ. Prokinetics in acute upper GI bleeding: a meta-analysis. *Gastrointest Endosc.* 2010 Dec;72(6):1138-45. doi: 10.1016/j.gie.2010.08.011. PMID: 20970794.

Question 14

A 45-year-old man presents to clinic with a chief complaint of refractory heartburn. Symptoms have persisted despite a transition from omeprazole to esomeprazole and subsequent dose escalation to 40 mg twice daily. He confirms medication adherence with appropriate pre-prandial dosing.

An upper endoscopy demonstrates Los Angeles Class C esophagitis at the gastroesophageal junction. An esophageal manometry demonstrates normal esophageal motility. A pH/impedance test performed while receiving acid suppression therapy demonstrates breakthrough reflux with an esophageal acid exposure time of 6.1%. Solid-phase gastric scintigraphy demonstrates 43% meal retention at 4 hours (normal <10%).

Which of the following is the next best step?

- A. Transition esomeprazole 40 mg twice daily to dexlansoprazole 60 mg daily
- B. Add famotidine 40 mg at bedtime
- C. Add metoclopramide 5 mg 4 times daily
- D. Add baclofen 5 mg 3 times daily
- E. Surgical referral for consideration of Nissen fundoplication

CORRECT ANSWER: C

RATIONALE

Gastroparesis is a potential contributor to gastroesophageal reflux disease symptoms that are refractory to acid-suppressive medications. In this case, a trial of prokinetic therapy may improve gastroesophageal reflux by mitigating the retention of gastric contents. Other medication adjustments including alternative proton pump inhibitors, adjunctive H₂-receptor antagonists like famotidine, and/or adjunctive baclofen to reduce the burden of transient lower esophageal sphincter relaxations are reasonable considerations for breakthrough gastroesophageal reflux disease but would not address the unique predisposition to reflux identified in this case. Antireflux surgery is a consideration when medical therapy fails but can predispose to gas-bloat syndrome in the setting of gastroparesis.

REFERENCE

Camilleri M, Parkman HP, Shafi MA, Abell TL, Gerson L; American College of Gastroenterology. Clinical guideline: management of gastroparesis. *Am J Gastroenterol*. 2013;108(1):18-38. doi:10.1038/ajg.2012.373

Question 15

Which of the following tests is considered the gold standard for diagnosing gastroparesis?

- A. Solid-phase gastric scintigraphy
- B. Liquid-phase gastric scintigraphy
- C. Dual-phase (solid and liquid) gastric scintigraphy
- D. [¹³C]-*Spirulina platensis* gastric emptying breath test
- E. Wireless motility capsule

CORRECT ANSWER: A

RATIONALE

A 4-hour solid-phase gastric scintigraphy is the consensus gold standard for evaluating gastric transit and diagnosing gastroparesis. This study often provides 1-, 2-, and 3-hour time point data as well, though it is the 4-hour time point that determines the diagnosis, with >10% meal retention indicative of delay. Two-hour solid-phase gastric scintigraphy studies that extrapolate a concentration half-life are nonstandard. Gastric emptying of liquids can be delayed as well, though this is less relevant to the overarching consensus diagnosis of gastroparesis. Dual-phase scintigraphy subsumes the information provided by solid-phase scintigraphy but is costlier and more technically complicated than the solid-phase scintigraphy. [¹³C]-*Spirulina platensis* gastric emptying breath test and wireless motility capsule testing have both been cross-validated with gastric scintigraphy but do not themselves represent the diagnostic standard.

REFERENCE

Abell TL, Camilleri M, Donohoe K, et al. Consensus recommendations for gastric emptying scintigraphy: a joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine. *Am J Gastroenterol*. 2008;103(3):753-763. doi:10.1111/j.1572-0241.2007.01636.x

Question 16

A 60-year-old man presents to clinic with nausea and early satiety. His past medical history is nota-

ble for longstanding type 2 diabetes (hemoglobin A1c, 10.0% [reference range, 4.0%-5.6%]). An upper endoscopy is normal, and a gastric scintigraphy is ordered. Before his nuclear medicine study, before ingesting the test meal, a nurse calls to advise that his blood glucose is over 300 mg/dL (reference range, 70-99 mg/dL).

If he proceeds with the scintigraphy in the absence of medications, what impact will his hyperglycemia have on the result relative to his native gastric transit?

- A. The measured gastric emptying time will be globally accelerated
- B. The measured gastric emptying time will be globally delayed
- C. This degree of hyperglycemia will have no impact on his measured gastric emptying time
- D. The measured gastric emptying time will be accelerated at 1 hour but not at 4 hours
- E. The measured gastric emptying time will be delayed at 1 hour but not at 4 hours

CORRECT ANSWER: B

RATIONALE

Acute hyperglycemia can lead to artifactual delays in gastric emptying time. This effect can be intuited on the basis of normal physiology: delayed gastric transit inhibits further glucose absorption in the setting of an elevated plasma glucose level to prevent that level's further escalation. Gastric transit evaluations in patients with diabetes should be deferred until relative euglycemia is achieved, often defined as a serum glucose value lower than 275 mg/dL.

REFERENCE

Camilleri M, Parkman HP, Shafi MA, Abell TL, Gerson L; American College of Gastroenterology. Clinical guideline: management of gastroparesis. *Am J Gastroenterol*. 2013;108(1):18-38. doi:10.1038/ajg.2012.373

Question 17

A 30-year-old woman presents to clinic with a 2-year history of heartburn and dysphagia. She denies nausea, early satiety, abdominal pain, weight loss, or altered bowel habits. She has been prescribed omeprazole 40 mg daily with partial relief. An upper endoscopy with esophageal biopsies is unremarkable. An esophageal manometry demonstrates ineffective esophageal motility with poor peristaltic reserve. A wireless pH probe demonstrates esophageal acid exposure of 7.1% off acid suppression therapy (normal, <4%). A solid-phase gastric scintigraphy demonstrates 8% meal retention at 4 hours (normal, <10%).

Which of the following is the next best step?

- A. Add metoclopramide 5 mg 4 times daily
- B. Add buspirone 5 mg 3 times daily
- C. Add baclofen 5 mg 3 times daily
- D. Increase omeprazole to 40 mg twice daily
- E. Refer to surgery for consideration of antireflux surgery

CORRECT ANSWER: D

RATIONALE

Ineffective esophageal motility is a manometric diagnosis of uncertain clinical significance but can be associated with dysphagia and an increased predisposition to gastroesophageal reflux disease. The mainstay of medical therapy is optimization of acid suppression therapy and behavioral intervention including chewing well and maintaining an upright posture for 2 to 3 hours after meals. Medications to accelerate transit (eg, metoclopramide) or to facilitate fundic relaxation (eg, buspirone) have not shown consistent symptom benefit in patients with isolated ineffective esophageal motility. Baclofen and antireflux surgery are salvage considerations for refractory gastroesophageal reflux disease but would not precede proton pump inhibitor dose optimization as management strategies.

REFERENCE

Gyawali CP, Sifrim D, Carlson DA, et al. Ineffective esophageal motility: Concepts, future directions, and conclusions from the Stanford 2018 symposium. *Neurogastroenterol Motil*. 2019;31(9):e13584. doi:10.1111/nmo.13584

Question 18

A 25-year-old woman presents to clinic with progressive nausea and early satiety. Her past medical and surgical history is notable for postural orthostatic tachycardia syndrome, irritable bowel syndrome with diarrhea, and biliary colic after uncomplicated cholecystectomy. On initial evaluation, her heart rate is 107 bpm, her blood pressure is 120/80 mmHg, and her body mass index is 25 kg/m². An upper endoscopy with biopsies is normal. A gastric scintigraphy demonstrates 20% meal retention at 1 hour and 0% meal retention at 2 hours, consistent with rapid gastric emptying.

In addition to dietary counseling, which of the following medications is a reasonable consideration?

- A. Metoclopramide
- B. Pyridostigmine
- C. Dicyclomine
- D. Tegaserod
- E. Eluxadoline

CORRECT ANSWER: C

RATIONALE

Rapid gastric emptying can present with symptoms similar to those among patients with gastroparesis or functional dyspepsia with normal gastric transit, including dyspepsia, nausea, and early satiety. Management strategies for rapid gastric emptying are not well established, though prokinetic medications (eg, metoclopramide, tegaserod) are best avoided given their potential to exacerbate symptoms. Pyridostigmine is sometimes used for relief of cardiovascular symptoms

in patients with autonomic dysfunction, in whom rapid emptying may be relatively more common, but may still exacerbate gastrointestinal symptoms in this case given its cholinergic effects. By contrast, anticholinergic medications like dicyclomine might offer symptomatic benefit by slowing transit. Eluxadoline is an opioid agonist that is approved by the US Food and Drug Administration for irritable bowel syndrome with diarrhea but contraindicated in the setting of cholecystectomy given an increased risk of pancreatitis.

REFERENCES

Camilleri M, Parkman HP, Shafi MA, Abell TL, Gerson L; American College of Gastroenterology. Clinical guideline: management of gastroparesis. *Am J Gastroenterol*. 2013;108(1):18-38. doi:10.1038/ajg.2012.373

Lawal A, Barboi A, Krasnow A, Hellman R, Jaradeh S, Massey BT. Rapid gastric emptying is more common than gastroparesis in patients with autonomic dysfunction. *Am J Gastroenterol*. 2007;102(3):618-623. doi:10.1111/j.1572-0241.2006.00946.x

Question 19

An 80-year-old man presents to clinic with a chief complaint of dysphagia and regurgitation over the past 3 months. His body mass index is 19 kg/m² after having lost 20 kilograms over the same interval. Past medical history is notable for gastroesophageal reflux disease, alcoholism, and chronic obstructive pulmonary disease in the setting of a 50-pack year smoking history. An upper endoscopy demonstrates food and fluid retention in the distal esophagus. An esophageal manometry demonstrates type 1 achalasia. His Eckardt score is 8. What is the next best step?

- A. Cross-sectional imaging of the chest
- B. Heller myotomy with partial fundoplication
- C. Impedance planimetry of the lower esophageal sphincter
- D. Per-oral endoscopic myotomy

- E. Botulinum toxin injection to the lower esophageal sphincter

CORRECT ANSWER: A

RATIONALE

This case raises concern for pseudoachalasia in the setting of an undiagnosed malignancy. It can be difficult to distinguish achalasia from pseudoachalasia clinically, but the latter should be suspected among patients presenting at an advanced age with rapid symptom onset and progression. In this patient's case, his smoking history and precipitous weight loss raise concern for an underlying pulmonary malignancy, perhaps small cell lung cancer, which can be associated with paraneoplastic phenomena. Alternatively, gastroesophageal reflux disease and alcoholism might predispose to an esophagogastric malignancy that might have been missed on endoscopic evaluation due to luminal occlusion. Heller myotomy, peroral endoscopic myotomy, and Botulinum toxin injection are all possible treatments for achalasia, but in this clinical context, malignancy must be ruled out first. Impedance planimetry (endo-FLIP) is a distension technology that assesses luminal geometry, mechanical properties including muscle dynamics, and processing of nociceptive signals from the gastrointestinal tract to measure pressure changes, diameter, and volume. It can be used to measure esophageal wall stiffness and the dynamics of esophagogastric junction opening, to help classify manometric abnormalities but has limited clinical availability and would not add much to this case, in which malignancy must be ruled out first.

REFERENCE

Donnan EN, Pandolfino JE. EndoFLIP in the Esophagus: Assessing Sphincter Function, Wall Stiffness, and Motility to Guide Treatment. *Gastroenterol Clin North Am*. 2020;49(3):427-435. doi:10.1016/j.gtc.2020.04.002

Gergely M, Mello MD, Rengarajan A, Gyawali CP. Duration of symptoms and manometric param-

eters offer clues to diagnosis of pseudoachalasia. *Neurogastroenterol Motil*. 2021;33(1):e13965. doi:10.1111/nmo.13965

Question 20

A 35-year-old woman presents to clinic with nausea, vomiting, and early satiety that have been present on a persistent basis for the past 3 months. She has no significant past medical or surgical history. Symptoms began abruptly after an episode of food poisoning that also affected her partner and 2 young children. Her family members' symptoms resolved after a few days, but her symptoms persisted. An upper endoscopy performed 1 month ago was normal. A gastric scintigraphy demonstrates 20% meal retention at 4 hours (normal, <10%).

Which of the following is an appropriate counseling statement?

- A. Her symptoms are likely to resolve with time
- B. Her symptoms are likely to worsen with time
- C. Repeat gastric scintigraphy in 1 year is likely to demonstrate a stable transit delay
- D. Response to prokinetic therapy reliably correlates with the severity of gastric emptying delay
- E. Symptom severity reliably correlates with the severity of gastric emptying delay

CORRECT ANSWER: A

RATIONALE

This patient has gastroparesis that is likely post-infectious in etiology. Although some cases of post-infectious gastroparesis can linger, the natural history tends to be favorable relative to other etiologies of gastroparesis, as symptoms tend to resolve on their own with time. Among all patients with gastroparesis, symptom severity and response to prokinetic therapy tend not to correlate reliably with the degree of gastric emptying delay. Also, among all patients with gastroparesis, scintigraphic findings tend to be unstable over time, with 1 recent study of patients with gastro-

paresis and functional dyspepsia demonstrating substantial cross-over after 1 year based on iterative gastric transit testing.

REFERENCES

Oh JJ, Kim CH. Gastroparesis after a presumed viral illness: clinical and laboratory features and natural history. *Mayo Clin Proc.* 1990;65(5):636-642. doi:10.1016/s0025-6196(12)65125-8

Pasricha PJ, Grover M, Yates KP, et al. Functional Dyspepsia and Gastroparesis in Tertiary Care are Interchangeable Syndromes With Common Clinical and Pathologic Features. *Gastroenterology.* 2021;160(6):2006-2017. doi:10.1053/j.gastro.2021.01.230

Question 21

An 18-year-old man presents to clinic with a chief complaint of vomiting. Symptoms have been present intermittently for the past year. Vomiting episodes are sudden and occur toward the end of meals without significant prodromal nausea or forceful retching. He is a freshman in college and sometimes rechews and re-swallows the food he brings up to avoid embarrassment when he is eating among friends. He denies early satiety, abdominal pain, or weight loss. Past medical history is notable for depression and anxiety which are well-managed on a selective serotonin reuptake inhibitor (SSRI). An upper endoscopy with esophageal, gastric, and duodenal biopsies is normal. Esophageal manometry, wireless pH monitoring off acid suppression therapy, and gastric scintigraphy are normal as well.

Which of the following is the most appropriate recommendation?

- A. Initiation of omeprazole twice daily
- B. Initiation of sucralfate 4 times daily
- C. Transition SSRI to SNRI (serotonin–norepinephrine reuptake inhibitor)
- D. Mindfulness-based stress reduction
- E. Diaphragmatic breathing

CORRECT ANSWER: E

RATIONALE

This patient presents with likely rumination syndrome. Supportive findings can be seen on esophageal manometry (so-called “rumination waves” or “R waves”) and pH/impedance testing but are not always present. Rumination syndrome is primarily a clinical diagnosis, clues to which in this case include the patient’s description of his “vomiting” episodes (passive regurgitation with intermittent re-mastication) and otherwise unremarkable diagnostic evaluation. The pathophysiology of rumination syndrome is thought to involve reflexive and involuntary contraction of the abdominal wall. The mainstay of treatment is diaphragmatic breathing, preventing rumination by restoring normal gastroesophageal pressure gradients.

REFERENCE

Absah I, Rishi A, Talley NJ, Katzka D, Halland M. Rumination syndrome: pathophysiology, diagnosis, and treatment. *Neurogastroenterol Motil.* 2017;29(4):10.1111/nmo.12954. doi:10.1111/nmo.12954

Question 22

A 30-year-old woman presents to clinic with a chief complaint of refractory heartburn. Symptoms have been present for the past year and have not responded to omeprazole 40 mg daily or pantoprazole 20 mg twice daily. She denies dysphagia, odynophagia, nausea, abdominal pain, or early satiety. Upper endoscopy, esophageal manometry, and gastric scintigraphy are normal. A pH/impedance study performed off acid suppression medication demonstrates an acid exposure time of 1.0% (normal, <4.0%) with no correlation between heartburn episodes and reflux events.

Which of the following is the next most appropriate step?

- A. Counsel regarding appropriate proton pump inhibitor dosing (30-60 minutes before meals)

- B. Increase pantoprazole to 40 mg twice daily
- C. Initiate sucralfate 4 times daily
- D. Initiate amitriptyline nightly
- E. Refer to surgery for consideration of antireflux surgery

CORRECT ANSWER: D

RATIONALE

This patient has functional heartburn on the basis of a normal diagnostic workup including endoscopy, manometry, and pH/impedance testing. Treatment options for functional heartburn are not well-validated, but data-supported interventions include neuromodulatory medications (including tricyclic antidepressants like amitriptyline) and hypnotherapy. Counseling regarding appropriate proton pump inhibitor dosing is a reasonable first step when addressing persistent symptoms of gastroesophageal reflux disease but will not help in this patient's case given her physiologic acid burden off acid suppression therapy. The other listed options are directed toward augmented management of gastroesophageal reflux disease and not appropriate next steps in this case for the same reason.

REFERENCE

Aziz Q, Fass R, Gyawali CP, Miwa H, Pandolfino JE, Zerbib F. Functional Esophageal Disorders [published online ahead of print, 2016 Feb 15]. *Gastroenterology*. 2016;S0016-5085(16)00178-5. doi:10.1053/j.gastro.2016.02.012

Question 23

What is the rough distribution of striated muscle in the esophagus under normal circumstances?

- A. Proximal third
- B. Proximal two-thirds
- C. Distal third
- D. Distal two-thirds
- E. Mixed throughout

CORRECT ANSWER: A

RATIONALE

The upper esophageal sphincter is composed primarily of striated (skeletal) muscle as it is under voluntary control. The proximal 35% to 40% of the esophageal body (identified as the transition zone on esophageal manometry) is composed of mixed striated and smooth muscle along a gradient, with progressively more smooth muscle present toward the distal end of this segment. The distal 50% to 60% of the esophagus is composed entirely of smooth muscle, which is not under voluntary control.

REFERENCE

Long JD, Orlando RC. Anatomy, Histology, Embryology, and Developmental Anomalies of the Esophagus. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver disease*, 10th ed. Elsevier, Inc. 2016:665-675.

Question 24

Which of the following statements is true regarding therapies directed toward the pylorus in gastroparesis?

- A. Randomized controlled trial data have shown botulin toxin injection to be superior to placebo
- B. Randomized controlled trial data have shown gastric per-oral endoscopic myotomy (G-POEM) to be superior to placebo
- C. G-POEM is associated with high likelihood of post-operative dumping syndrome
- D. The effects of botulinum toxin injection are temporary
- E. Transpyloric stents are associated with high rates of technical and clinical success

CORRECT ANSWER: D

RATIONALE

Pyloric dysfunction is estimated to be a relevant pathophysiologic mechanism in approximately 30% of all patients with gastroparesis. A number

of treatment strategies directed toward pyloric dysfunction have been studied in recent years, including botulinum toxin injection, transpyloric stent placement, and G-POEM. Randomized controlled trials have been performed on botulinum toxin injection and showed no significant benefit over placebo, though these studies were likely underpowered. G-POEM has shown durable benefit in case series, but randomized controlled trial data are not yet available. G-POEM is not associated with significant risk of dumping syndrome. Transpyloric stent placement has fallen out of favor for multiple reasons, including high rates of technical failure mediated by stent migration. The effects of botulinum toxin injection are necessarily temporary, with a median duration of efficacy of around 2 months.

REFERENCES

Abdelfatah MM, Noll A, Kapil N, et al. Long-term Outcome of Gastric Per-Oral Endoscopic Pyloromyotomy in Treatment of Gastroparesis. *Clin Gastroenterol Hepatol*. 2021;19(4):816-824. doi:10.1016/j.cgh.2020.05.039

Ahuja NK, Clarke JO. Pyloric Therapies for Gastroparesis. *Curr Treat Options Gastroenterol*. 2017;15(1):230-240. doi:10.1007/s11938-017-0124-4

Question 25

Which of the following as-needed medications should ideally be withheld within 48 to 72 hours of obtaining a gastric scintigraphy?

- A. Omeprazole
- B. Acetaminophen
- C. Hydromorphone
- D. Naproxen
- E. Polyethylene glycol

CORRECT ANSWER: C

RATIONALE

Numerous medications can affect gastrointestinal motility. Such medications are generally recom-

mended to be withheld from patients, if possible, for 2 to 3 days in advance of formalized transit testing to avoid spurious findings. Opioid medications like hydromorphone are among the most obvious agents with deleterious effects on motility.

REFERENCES

Camilleri M, Parkman HP, Shafi MA, Abell TL, Gerson L; American College of Gastroenterology. Clinical guideline: management of gastroparesis. *Am J Gastroenterol*. 2013;108(1):18-38. doi:10.1038/ajg.2012.373

Question 26

A 58-year-old woman with a history significant for systemic sclerosis and type 2 diabetes being treated with insulin therapy presents with 6 months of abdominal bloating and diarrhea. Diagnostic evaluation, including infectious stool studies, thyroid studies, tissue transglutaminase IgA antibody, total IgA, and ileocolonoscopy with random colon biopsies, reveals no abnormalities.

What is the next best step in evaluation of her symptoms?

- A. Fecal calprotectin
- B. Glucose hydrogen breath test
- C. Serum *Helicobacter pylori* antibody
- D. IgA endomysial antibody

CORRECT ANSWER: B

RATIONALE

This patient should be tested for small bowel bacterial overgrowth (SIBO). She has symptoms (abdominal bloating and diarrhea) consistent with SIBO in the setting of risk factors for SIBO (diabetes and scleroderma). Glucose hydrogen or lactulose hydrogen breath testing is recommended for the diagnosis of SIBO in symptomatic patients. Fecal calprotectin to evaluate for inflammatory bowel disease would not provide additional information in this patient, who recently had a reassuring ileocolonoscopy. As she had a negative

tissue transglutaminase IgA antibody test, an IgA endomysial antibody test is not indicated at this time to evaluate for celiac disease.

REFERENCE

Pimentel M, Saad RJ, Long MD, Rao SSC. ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth. *Am J Gastroenterol*. 2020;115(2):165-178. doi:10.14309/ajg.0000000000000501

Question 27

A 60-year-old man with a history of amyloidosis presents with 3 months of abdominal bloating and flatulence. Diagnostic evaluation reveals an increase in breath hydrogen by 22 ppm at 60 minutes during a glucose hydrogen breath test.

Which medication is most likely to be prescribed for this patient?

- A. Diphenoxylate
- B. Loperamide
- C. Psyllium
- D. Rifaximin
- E. Simethicone

CORRECT ANSWER: D

RATIONALE

This patient has amyloidosis, which represents a risk factor for small bowel bacterial overgrowth (SIBO). Glucose hydrogen breath test is a diagnostic test for SIBO, when the hydrogen increases by at least 20 ppm by 90 minutes after ingesting 75 g of glucose. The recommended treatment for SIBO is antibiotic therapy in symptomatic patients to eradicate overgrowth and resolve associated symptoms. Out of the options above, rifaximin is the only medication listed used to treat SIBO.

REFERENCE

Pimentel M, Saad RJ, Long MD, Rao SSC. ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth. *Am J Gastroenterol*. 2020;115(2):165-178. doi:10.14309/ajg.0000000000000501

Question 28

A 70-year-old man with coronary artery disease and small-cell lung cancer presents with 2 months of progressively worsening abdominal pain, distension, and unintentional weight loss. After reassuring bidirectional endoscopy, a small bowel follow-through barium study shows delayed small bowel transit and small bowel dilation. Abdominal/pelvic computed tomography with contrast does not show an obstructing lesion or transition point.

Which test is most likely to be abnormal in this patient?

- A. Anti-Hu antibody
- B. Anti-nuclear antibody
- C. Anti-smooth muscle antibody
- D. Anti-mitochondrial antibody

CORRECT ANSWER A

RATIONALE

This patient has intestinal pseudo-obstruction due to a paraneoplastic syndrome from his small-cell lung cancer, causing inflammatory infiltration and destruction of the enteric nervous system. Malignancies that can cause this include small-cell carcinoma (most common), carcinoid, Hodgkin lymphoma, ovarian carcinoma, and renal cell carcinoma. The process occurs due to circulating IgG antibodies that cross-react with neurons of the enteric nervous system and tumor antigens. The most commonly detected antibodies are the anti-Hu or anti-neuronal nuclear antibody 1. Anti-nuclear antibody (answer B) is a nonspecific autoantigen that is found in many autoimmune conditions including lupus. Anti-smooth muscle antibody (answer C) is found in autoimmune hepatitis, and anti-mitochondrial antibody (answer D) is found in primary biliary cholangitis.

REFERENCES

Hirano I, Pandolfino J. Chronic intestinal pseudo-obstruction. *Dig Dis*. 2000;18(2):83-92. doi:10.1159/000016969

Pasumathy L, Katari V, Srour J. Paraneoplastic Gastrointestinal Dysmotility-A Manifestation of Small Cell Lung Cancer: 494. *Am J Gastroenterol*. 2011;106:S191.

Question 29

A 50-year-old man presents to your office with 2 months of progressive dysphagia, abdominal distension, and constipation. He previously lived in Brazil for a number of years. On diagnostic evaluation with esophageal high-resolution manometry and cross-sectional imaging, he is found to have achalasia and megacolon.

Which organism is the most likely the cause of his symptoms?

- A. *Cryptosporidium*
- B. *Entamoeba histolytica*
- C. *Giardia lamblia*
- D. *Trypanosoma cruzi*

CORRECT ANSWER: D

RATIONALE

Chagas disease is endemic to certain regions of Central and South America. It is caused by the protozoan *Trypanosoma cruzi* and leads to degeneration and loss of enteric neurons. Gastrointestinal complications of chronic Chagas disease can cause achalasia, gastroparesis, small bowel dysmotility, and/or megacolon. The other parasites listed here primarily cause diarrhea and are not typically associated with achalasia or megacolon.

REFERENCE

Matsuda NM, Miller SM, Evora PR. The chronic gastrointestinal manifestations of Chagas disease. *Clinics (Sao Paulo)*. 2009;64(12):1219-1224. doi:10.1590/S1807-59322009001200013

Question 30

A 67-year-old woman with type 2 diabetes being treated with insulin therapy, coronary artery

disease, and a body mass index of 45 kg/m² presents to your office with 1 year of nonprogressive abdominal pain and constipation. After completing a thorough evaluation, she is diagnosed with irritable bowel syndrome with constipation.

Which of the following medications is contraindicated for this patient?

- A. Linaclotide
- B. Lubiprostone
- C. Prucalopride
- D. Tegaserod

CORRECT ANSWER: D

RATIONALE

All of the listed medications can be used to treat irritable bowel syndrome with constipation. However, tegaserod is contraindicated in patients with more than 1 cardiovascular risk factor, due to an increased risk of major adverse cardiac events. This patient's history of coronary artery disease, diabetes, age greater than 55 years, and body mass index greater than 30 kg/m² are all considered cardiovascular risk factors; therefore, tegaserod is contraindicated. Linaclotide, lubiprostone, and prucalopride can all be used for constipation and are not contraindicated in the setting of cardiac risk factors.

REFERENCE

Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036

Question 31

A 56-year-old woman with no significant past medical history presents for evaluation of chronic constipation. She has tried multiple different laxatives without improvement. She describes abdominal bloating, straining with defecation, and a sensation of incomplete evacuation. A colonoscopy was normal. She underwent anorectal manom-

etry, which revealed a high resting anal sphincter pressure (90 mmHg), high squeeze pressure (225 mmHg), and no change in the anal sphincter pressure during strain or bear down maneuver. There was normal relaxation of the anal sphincter with balloon distention in the rectum. The rectal sensation testing showed a slightly elevated first sensation pressure (50 mmHg). She could not expel the 50 mL balloon in 2 minutes.

Which of the following is the most important diagnostic information for obstructive defecation?

- A. Resting anal sphincter pressure of 90 mmHg
- B. High squeeze pressure (225 mmHg)
- C. Elevated first sensation pressure (50 mmHg)
- D. Inability to expel the balloon in 2 minutes
- E. Relaxation of the anal sphincter with balloon distention in the rectum

CORRECT ANSWER: D

RATIONALE

Failed balloon expulsion test (answer D) has been found to correlate with a defecatory disorder and predict response to biofeedback therapy. Anal sphincter tone (answer A) and squeeze pressure (answer B) are most useful in the evaluation of fecal incontinence, but play less of a role in the assessment of obstructive defecation. Rectal sensation testing (answer C) may be abnormal in constipation, with rectal hyposensitivity causing a decrease in the urge for defecation. However, it alone is not associated with obstructive defecation. Rectoanal inhibitory reflex (RAIR; answer E) is used as an assessment of normal colonic innervation and would be abnormal in patients with Hirschsprung disease.

REFERENCE

Carrington EV, Scott SM, Bharucha A, et al. Expert consensus document: Advances in the evaluation of anorectal function. *Nat Rev Gastroenterol Hepatol*. 2018;15(5):309-323. doi:10.1038/nrgastro.2018.27

Question 32

A 30-year-old man with type 2 diabetes presents to your office with nonprogressive watery diarrhea up to 6 times daily that has occurred intermittently for the last 9 months. He denies rectal bleeding, weight loss, fevers, recent travel, sick contacts, or new medications. Complete blood count, basic metabolic profile, and thyroid studies checked by his primary care doctor were normal.

Which of the following diagnostic tests would be least helpful in elucidating the cause of this patient's diarrhea?

- A. Cortisol level
- B. C-reactive protein
- C. Fecal calprotectin
- D. Tissue transglutaminase IgA antibody

CORRECT ANSWER: A

RATIONALE

In patients presenting with diarrhea due to suspected irritable bowel syndrome, celiac disease should be excluded with a tissue transglutaminase IgA antibody (and total IgA), and inflammatory bowel disease should be excluded with fecal calprotectin and C-reactive protein. Although adrenal insufficiency can cause diarrhea, there is no reason to suspect this diagnosis in this case, especially with normal electrolytes.

REFERENCE

Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036

Question 33

A 22-year-old woman underwent anorectal manometry for chronic constipation refractory to multiple laxatives. The anorectal manometry showed an increase in resting anal sphincter pressure (83 mmHg), normal squeeze pressure (180 mmHg), normal rectal contraction pressure (50

mmHg), increased residual pressure during simulated defecation (85 mmHg), and no relaxation of the anal sphincter during balloon distention. The sensation testing showed a mildly elevated first sensation pressure (50 mmHg). She could not expel the 50 mL balloon in 2 minutes.

What is the best next step?

- A. Biofeedback therapy
- B. Botulinum toxin injection to the anal sphincter
- C. Referral for anal sphincterotomy
- D. Magnetic resonance imaging of the pelvis
- E. Deep suction rectal biopsies

CORRECT ANSWER: E

RATIONALE

The anorectal manometry showed an absent recto-anal inhibitory reflex (RAIR), defined by the lack of anal sphincter relaxation with balloon distention in the rectum. A normal RAIR depends on a functioning neural circuitry in the rectum and anal sphincters. An absent RAIR, therefore, should raise suspicion for Hirschsprung's disease, characterized by agangliosis in the affected segment of the distal colon. While other findings on this patient's anorectal manometry may also suggest a spastic anal sphincter (increased resting tone) or dyssynergic defecation (lack of sphincter relaxation with simulated defecation), confirmatory testing for Hirschsprung's disease with deep suction rectal biopsies (answer E) should first be performed in the absence of normal RAIR. Deep suction rectal biopsies would show absent ganglion cells and hypertrophy of nerve fibers in patients with Hirschsprung disease. Biofeedback therapy (answer A) is the treatment of choice for dyssynergic defecation. Injection of botulinum toxin into the anal sphincter (answer B) has been tried with mixed results; there was some improvement in less than one-half of patients in studies, but troublesome incontinence occurred in one study. It may be more effective in children, and in adults is more commonly used in the treatment of anal fissures, as is anal sphincterotomy (answer

C). MRI of the pelvis (answer D) may be used to rule out masses or abscesses if these were suspected, but not in this case.

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Kahn E, Daum F. Anatomy, Histology, Embryology, and Developmental Anomalies of the Small and Large Intestine. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*, 10th ed. Elsevier, Inc; 2010:1615-1642.

Meinds RJ, Trzpis M, Broens PMA. Anorectal Manometry May Reduce the Number of Rectal Suction Biopsy Procedures Needed to Diagnose Hirschsprung Disease. *J Pediatr Gastroenterol Nutr*. 2018 Sep;67(3):322-327. doi: 10.1097/MPG.0000000000002000. PMID: 29652729.

Rao SS, Patcharatrakul T. Diagnosis and Treatment of Dyssynergic Defecation. *J Neurogastroenterol Motil*. 2016;22(3):423-435. doi:10.5056/jnm16060

Question 34

A 50-year-old woman with a history of coronary artery disease, pancreatitis, and asthma presents to your clinic with 7 months of watery diarrhea. After evaluation that included labwork and colonoscopy with random biopsies, she is diagnosed with irritable bowel syndrome with diarrhea (IBS-D).

Which of the following medications is contraindicated for this patient?

- A. Alosetron
- B. Eluxadoline
- C. Loperamide
- D. Rifaximin

CORRECT ANSWER: B

RATIONALE

All of the medications listed above are recommended to treat IBS-D. Eluxadoline is a peripher-

ally acting, mixed mu- and kappa-opioid receptor agonist/delta-opioid receptor antagonist used to treat IBS-D. However, in clinical trials, pancreatitis was a significant adverse event. Eluxadoline is contraindicated in patients with a history of biliary duct obstruction, severe hepatic impairment, prior cholecystectomy, pancreatitis, or sphincter of Oddi dysfunction.

REFERENCE

Lembo AJ, Lacy BE, Zuckerman MJ, et al. Eluxadoline for Irritable Bowel Syndrome with Diarrhea. *N Engl J Med*. 2016;374(3):242-253. doi:10.1056/NEJMoa1505180

Question 35

A 45-year-old woman diagnosed with irritable bowel syndrome with diarrhea presents to your clinic. Her diarrhea is well controlled with loperamide, but her abdominal pain persists. Her primary care provider previously prescribed dicyclomine, but this did not improve her abdominal pain symptoms.

What is the next best medication to treat her abdominal pain?

- A. Amitriptyline
- B. Codeine/acetaminophen
- C. Hydrocodone
- D. Meloxicam

CORRECT ANSWER: A

RATIONALE

Amitriptyline is a tricyclic antidepressant medication that functions as a central neuromodulator. A systematic review of randomized controlled trials of 6- to 12-weeks' duration showed a modest improvement in global symptom relief and abdominal pain in patients with IBS treated with tricyclic anti-depressants. Opioid medications and nonsteroidal antiinflammatory medications are not recommended to treat abdominal pain in patients with IBS.

REFERENCE

Weinberg DS, Smalley W, Heidelbaugh JJ, Sultan S; American Gastroenterological Association. American Gastroenterological Association Institute Guideline on the pharmacological management of irritable bowel syndrome. *Gastroenterology*. 2014;147(5):1146-1148. doi:10.1053/j.gastro.2014.09.001

Question 36

A 57-year-old woman presented with chronic constipation for the last 8 years, refractory to multiple laxatives. Complete blood count and thyroid tests are normal. A colonoscopy revealed melanosis coli but no other findings. A radiopaque marker test was obtained with 17 markers retained on day 5 of the study (4 in ascending, 5 in transverse, 5 in descending, and 3 in rectosigmoid). She is interested in surgical options for treatment of her chronic constipation.

Which of the following would be a negative predictor of surgical outcome?

- A. Expulsion of 50 mL balloon in 30 seconds
- B. Melanosis coli on colonoscopy
- C. Decreased anal sphincter squeeze pressure on manometry
- D. Increased small intestinal transit time on wireless motility capsule study
- E. Retained radiopaque markers in the ascending and transverse colon

CORRECT ANSWER: D

RATIONALE

The radiopaque marker study revealed 17 markers retained throughout the colon (reference range, ≥ 5), suggesting significantly delayed colonic transit. Colectomy with ileorectal anastomosis is the primary surgical treatment for severe slow transit constipation. However, presence of an upper gastrointestinal motility disorder (eg, delayed gastric emptying and/or small intestinal transit [answer D]) is a negative predictor for col-

ectomy, as patients may continue to experience symptoms related to extracolonic dysmotility. Concomitant defecation disorder should also be addressed before construction of ileorectal anastomosis. A weak external anal sphincter (answer C) found on anorectal manometry and a normal balloon expulsion test (answer A) are not associated with worse surgical outcomes for colectomy with ileorectal anastomosis. Retained radiopaque markers in the ascending and transverse colon (answer E) suggest severe slow transit constipation for which colectomy is indicated. Melanosis coli on colonoscopy (answer B) is a benign finding secondary to chronic laxative use and is not associated with surgical outcome. When evaluating patients for colectomy for severe slow-transit constipation, upper gastrointestinal motility assessment (eg, gastric emptying scintigraphy, fluoroscopic upper gastrointestinal series, wireless motility capsule) and evaluation of defecatory function (anorectal manometry) should be performed before surgery.

REFERENCES

American Gastroenterological Association, Bharucha AE, Dorn SD, Lembo A, Pressman A. American Gastroenterological Association medical position statement on constipation. *Gastroenterology*. 2013;144(1):211-217. doi:10.1053/j.gastro.2012.10.029

Kim ER, Rhee PL. How to interpret a functional or motility test - colon transit study. *J Neurogastroenterol Motil*. 2012;18(1):94-99. doi:10.5056/jnm.2012.18.1.94

Question 37

Which of the following diets has the strongest clinical trial data supporting its efficacy in reducing the global symptoms of irritable bowel syndrome?

- A. Elimination of FODMAPs
- B. Elimination of gluten
- C. Elimination of lactose
- D. Elimination of long chain fatty acids

CORRECT ANSWER: A

RATIONALE

Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) lead to increased water secretion and fermentation in the colon, producing gases that can cause luminal distension. In a recent meta-analysis of randomized controlled trials, the low FODMAP diet was associated with a significant reduction in global irritable bowel syndrome symptoms compared with comparators.

REFERENCE

Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036

Question 38

What is the major excitatory neurotransmitter of the enteric nervous system?

- A. Acetylcholine
- B. Dopamine
- C. Nitric oxide
- D. Vasoactive intestinal peptide

CORRECT ANSWER: A

RATIONALE

The enteric nervous system spans the esophagus down to the internal anal sphincter. Acetylcholine and tachykinins are the major excitatory transmitters of the enteric nervous system. Nitric oxide and vasoactive intestinal peptide are the primary inhibitory transmitters.

REFERENCE

Schneider S, Wright CM, Heuckeroth RO. Unexpected Roles for the Second Brain: Enteric Nervous System as Master Regulator of Bowel Function. *Annu Rev Physiol*. 2019;81:235-259. doi:10.1146/annurev-physiol-021317-121515

Question 39

Which of the following best describes the ileal brake as it relates to gastrointestinal motility?

- A. Fat contents in the ileum delay gastric emptying into the small intestine
- B. Fat contents in the ileum delay small intestine emptying into the colon
- C. Fat contents in the ileum increase gastric emptying into the small intestine
- D. Fat contents in the ileum increase small intestine emptying into the colon

CORRECT ANSWER: A

RATIONALE

The distal portion of the small intestine participates in regulating gastric and upper small intestine motility in a phenomenon known as the ileal brake. The “ileal brake” is the primary inhibitory feedback mechanism to control transit of a meal through the gastrointestinal tract in order to optimize nutrient digestion and absorption. Activation of the ileal brake mechanism occurs when lipids in the ileum propagate a negative feedback mechanism that inhibits the emptying of nutrients from the stomach. This slows gastric emptying and delays transit of nutrients through the duodenum and jejunum, which in turn may place a ‘brake’ on hunger and food intake.

REFERENCE

Shin HS, Ingram JR, McGill AT, Poppitt SD. Lipids, CHOs, proteins: can all macronutrients put a ‘brake’ on eating?. *Physiol Behav.* 2013;120:114-123. doi:10.1016/j.physbeh.2013.07.008

Question 40

In a healthy individual, what is the average mouth-to-cecum transit time and average transit time through the colon?

- A. 12 hours and 12 hours
- B. 12 hours and 24 hours

- C. 6 hours and 24 hours
- D. 6 hours and 36 hours

CORRECT ANSWER: D

RATIONALE

In a healthy individual, the average mouth-to-cecum transit time is 6 hours, and transit times through the right colon, left colon, and sigmoid colon are approximately 12 hours each.

REFERENCE

Kim ER, Rhee PL. How to interpret a functional or motility test - colon transit study. *J Neurogastroenterol Motil.* 2012;18(1):94-99. doi:10.5056/jnm.2012.18.1.94

Question 41

When and how often does the migrating motor complex (MMC) cycle in the small intestine?

- A. The MMC cycles in the fed state every 30-60 minutes
- B. The MMC cycles in the fasting state every 30-60 minutes
- C. The MMC cycles in the fasting state every 90-120 minutes
- D. The MMC cycles in the fed state every 90-120 minutes

CORRECT ANSWER: C

RATIONALE

There are 2 distinct motility patterns in the small intestine: the fed and fasting pattern. In the fed pattern, nonpropagated focal contractions of intestine occur simultaneously at multiple levels. On average, the fed pattern lasts for 4 to 6 hours after a meal and is replaced by the fasting MMC pattern. The MMC cycles every 90 to 120 minutes in the fasting state and functions as the “house-keeping” mechanism, propelling undigested food residue and sloughed enterocytes caudally, and is regulated by cholinergic neurons of the enteric

nervous system. Absence of MMC has been associated with gastroparesis, intestinal pseudo-obstruction, and small intestinal bacterial overgrowth.

REFERENCE

Deloose E, Janssen P, Depoortere I, Tack J. The migrating motor complex: control mechanisms and its role in health and disease. *Nat Rev Gastroenterol Hepatol*. 2012;9(5):271-285. Published 2012 Mar 27. doi:10.1038/nrgastro.2012.57

Question 42

Distention of the rectum results in the rectoanal inhibitory reflex (RAIR).

Which of the following best describes the RAIR?

- A. Contraction of the internal anal sphincter
- B. Contraction of the puborectalis muscle
- C. Relaxation of the external anal sphincter
- D. Relaxation of the internal anal sphincter

CORRECT ANSWER: D

RATIONALE

Distention of the rectum causes the RAIR or relaxation of the internal anal sphincter. This occurs simultaneously with voluntary contraction of the external anal sphincter to maintain continence. Relaxation of the internal anal sphincter allows anal sphincter sampling of rectal contents to differentiate between solid, liquid, and gas contents. The RAIR is a major component in maintaining continence, and an abnormal response has been implicated in defecation disorders. Absent RAIR is seen in Hirschsprung disease.

REFERENCE

Cheeeney G, Nguyen M, Valestin J, Rao SS. Topographic and manometric characterization of the recto-anal inhibitory reflex. *Neurogastroenterol Motil*. 2012;24(3):e147-e154. doi:10.1111/j.1365-2982.2011.01857.x

Question 43

A 35-year-old woman with irritable bowel syndrome with constipation (IBS-C) presents for second opinion. Despite pharmacologic treatment with multiple agents for her constipation, she continues to report straining with defecation and requiring digital disimpaction in order to initiate a bowel movement.

Which of the following tests is most likely to elucidate the cause of her ongoing symptoms?

Abdominal and pelvic computed tomography with contrast

Anorectal manometry with balloon expulsion

Lactulose hydrogen breath testing

Small bowel follow-through

CORRECT ANSWER: B

RATIONALE

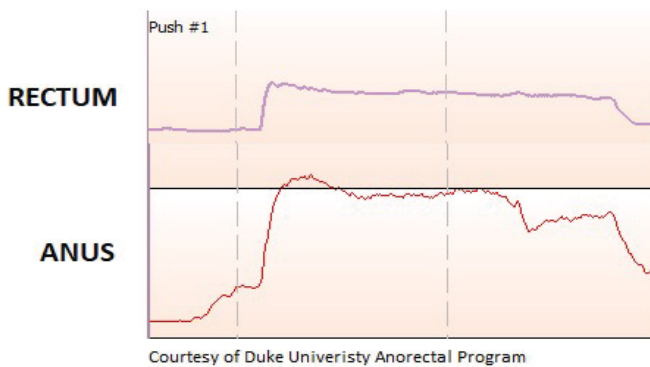
In addition to IBS, this patient likely also has dys-synergic defecation. Although the true prevalence of anorectal dysfunction in IBS is unknown, it occurs in all subtypes of IBS (IBS-D, IBS-C, and IBS-M) with prevalence rates estimated to be as high as 40% in tertiary care practices. Anorectal physiology testing should be performed in patients with IBS and symptoms suggestive of a pelvic floor disorder and/or refractory constipation not responsive to standard medical therapy. The other tests listed would not help diagnose dyssynergic defecation.

REFERENCE

Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036

Question 44

A 40-year-old man with constipation is referred for anorectal manometry. On the following page is the tracing that is obtained when he is asked to bear down in attempted defecation.



What diagnosis is this most consistent with?

- A. Anal fissure
- B. Dyssynergic defecation
- C. Rectal prolapse
- D. Rectocele

CORRECT ANSWER: B

RATIONALE

The tracing above is illustrative of dyssynergic defecation. Normally, when a patient attempts to defecate, there is a rise in rectal pressure, which is synchronized with a relaxation of the external anal sphincter. This patient instead has paradoxical contraction of the anal sphincter, consistent with dyssynergic defecation.

REFERENCE

Rao SS. Dyssynergic defecation. *Gastroenterol Clin North Am*. 2001;30(1):97-114. doi:10.1016/s0889-8553(05)70169-2

Question 45

A 54-year-old woman presents for evaluation of fecal incontinence. She describes a sudden urge for bowel movements but difficulty holding long enough to get to the bathroom, resulting in leakage of stools. She also reports leakage of a small amount of fecal material when she coughs and laughs but denies seepage without awareness. A flexible sigmoidoscopy performed did not reveal any abnormalities within the rectum. She then underwent anorectal manometry for further evaluation.

Which of the following is the most likely finding on anorectal manometry for this patient?

- A. Decreased anal sphincter squeeze pressure
- B. Increased rectal sensation volume
- C. No change in anal sphincter pressure with balloon distension in the rectum
- D. Decreased anal sphincter resting pressure
- E. Increased anal sphincter pressure during straining

CORRECT ANSWER: A

RATIONALE

Anal sphincter squeeze pressure measures the voluntary contraction of the external anal sphincter (EAS), while the anal sphincter resting pressure reflects the tonically active internal anal sphincter (IAS). The EAS reflexively contracts during actions associated with increased intraabdominal pressure (eg, coughing, laughing) to maintain continence. It is also under voluntary control to “hold” when an urge for defecation is felt. The patient in question suffers from symptoms suggestive of urge incontinence, which is likely due to weakness in the EAS. Therefore, her anorectal manometry would likely show a decrease in anal sphincter squeeze pressure (answer A). Weakness in the IAS, characterized by decreased anal sphincter resting pressure (answer D), would result in passive stool leakage without sensation. Hyposensitivity of the rectum (answer B), absent RAIR as in Hirschsprung disease (answer C), and dyssynergic defecation (answer E) can sometimes be associated with stool impaction and overflow incontinence, also characterized by silent, passive leakage of stools.

REFERENCE

Carrington EV, Scott SM, Bharucha A, et al. Expert consensus document: Advances in the evaluation of anorectal function. *Nat Rev Gastroenterol Hepatol*. 2018;15(5):309-323. doi:10.1038/nrgastro.2018.27

Question 46

The presence of the rectal anal inhibitory reflex (RAIR) on anorectal manometry excludes which diagnosis?

- A. Anal fissure
- B. Dyssynergic defecation
- C. Hirschsprung disease
- D. Irritable bowel syndrome

CORRECT ANSWER: C

RATIONALE

Hirschsprung's disease is a rare cause of constipation caused by a functional obstruction secondary to the absence of the myenteric ganglion cells in the affected portion of the distal colon. During anorectal manometry in healthy individuals, rectal balloon stimulation is followed by a RAIR, in which the internal anal sphincter relaxes. In patients with Hirschsprung disease, however, the RAIR is absent. A RAIR found during anorectal manometry excludes Hirschsprung disease. The presence of RAIR would not exclude the other conditions listed.

REFERENCE

de Lorijn F, Kremer LC, Reitsma JB, Benninga MA. Diagnostic tests in Hirschsprung disease: a systematic review. *J Pediatr Gastroenterol Nutr.* 2006;42(5):496-505. doi:10.1097/01.mpg.0000214164.90939.92

Question 47

A 45-year-old man with chronic constipation has had an evaluation including laboratory work, colonoscopy, and anorectal manometry, which were all normal. A trial of fiber and laxatives has provided an inadequate response. A sitz marker study is ordered with an abdominal radiograph obtained 5 days after 24 markers are ingested. Twelve markers are seen scattered throughout the colon on day 5.

What is the most likely diagnosis?

- A. Normal transit constipation
- B. Slow transit constipation
- C. Type I dyssynergic defecation
- D. Type IV dyssynergic defecation

CORRECT ANSWER: B

RATIONALE

In patients with chronic constipation with laboratory work, structural evaluation, and anorectal manometry that are normal, colon transit time should be evaluated. A sitz marker study entails checking an abdominal radiograph 5 days after 20 or 24 markers are ingested. Colonic transit is considered normal if more than 80% of markers have been passed. If more than 20% of markers remain, this is indicative of slow transit constipation. The normal anorectal manometry study in this patient makes dyssynergic defecation unlikely.

REFERENCE

Bharucha AE, Lacy BE. Mechanisms, Evaluation, and Management of Chronic Constipation. *Gastroenterology.* 2020;158(5):1232-1249.e3. doi:10.1053/j.gastro.2019.12.034

Question 48

A 63-year-old woman is evaluated for chronic constipation for the last 10 years, not responsive to polyethylene glycol and linaclotide at escalating doses. A recent colonoscopy revealed moderate internal hemorrhoids but was otherwise normal. Colonic radioopaque marker test is performed and reveals 10 markers remaining at day 5, all of them in the rectosigmoid colon.

What is the next best step?

- A. Subtotal colectomy with ileorectal anastomosis
- B. Computed tomography of abdomen and pelvis
- C. Lubiprostone
- D. Psyllium
- E. Anorectal manometry with balloon expulsion test

CORRECT ANSWER: E**RATIONALE**

The radiopaque marker study is abnormal when more than 5 markers (or 20% of those ingested) are retained in the colon on day 5 after ingestion. However, most of the retained markers in this patient were in the rectosigmoid area, suggesting some level of colonic outlet obstruction. The next step is to perform high-resolution anorectal manometry to assess for anorectal function abnormalities such as dyssynergic defecation. Subtotal colectomy with ileorectal anastomosis (answer A) is a reasonable option for patients with severe, medication refractory slow-transit constipation, but given the markers are all in the left colon, this is more consistent with a defecatory disorder than slow-transit constipation. Computed tomography (answer B) would not be helpful or warranted in the workup of constipation. Lubiprostone (answer C) is a good option for treatment but would rule out a defecatory disorder first given the marker study findings. Psyllium (answer D) is unlikely to work in a patient who is refractory to multiple laxatives.

REFERENCE

Kim ER, Rhee PL. How to interpret a functional or motility test - colon transit study. *J Neurogastroenterol Motil*. 2012;18(1):94-99. doi:10.5056/jnm.2012.18.1.94

Question 49

You are consulted on a 75-year-old man who was admitted to the hospital 1 week ago after hip replacement surgery. He has not had a bowel movement since his surgery. Cross-sectional imaging is significant for diffuse colonic dilation without transition point or obstructing lesion seen. Nasogastric and rectal decompression tubes do not provide improvement on serial radiographs.

Which is the best next step in management?

- A. Intravenous erythromycin
- B. Intravenous metoclopramide

- C. Intravenous neostigmine
- D. Intravenous ondansetron

CORRECT ANSWER: C**RATIONALE**

Acute colonic pseudo-obstruction presents with significant colonic dilation in the absence of mechanical obstruction. It is most commonly seen in hospitalized patients, particularly postoperatively. A meta-analysis showed intravenous neostigmine, an acetylcholinesterase inhibitor, is efficacious in the short-term treatment of acute intestinal pseudo-obstruction. The other medications listed are not recommended to treat colonic pseudo-obstruction.

REFERENCE

Valle RG, Godoy FL. Neostigmine for acute colonic pseudo-obstruction: A meta-analysis. *Ann Med Surg (Lond)*. 2014;3(3):60-64. Published 2014 Jun 19. doi:10.1016/j.amsu.2014.04.002

Question 50

A hospitalized 75-year-old man is prescribed intravenous neostigmine for acute colonic pseudo-obstruction.

What other medication should readily be available to treat the possible adverse effects of neostigmine?

- A. Adenosine
- B. Amiodarone
- C. Atropine
- D. Epinephrine

CORRECT ANSWER: C**RATIONALE**

Neostigmine is an acetylcholinesterase inhibitor used in the short-term treatment of acute intestinal pseudo-obstruction. It can cause bradycardia and hypotension, especially when used intravenously. Heart rate and blood pressure should be

monitored closely, and atropine should be available to reverse the effects in the event of cardiovascular compromise.

REFERENCE

Smedley LW, Foster DB, Barthol CA, Hall R, Gutierrez GC. Safety and Efficacy of Intermittent Bolus and Continuous Infusion Neostigmine for Acute Colonic Pseudo-Obstruction. *J Intensive Care Med.* 2020;35(10):1039-1043. doi:10.1177/0885066618809010

CHAPTER 12

Lower gastrointestinal bleeding

Michelle Hughes, MD and Hamita Sachar, MD

Laboratory Test	Result	Reference Range
Blood urea nitrogen (BUN), serum or plasma, mg/dL	12	8-20
Creatinine, serum, mg/dL	0.7	0.7-1.5
Hemoglobin, blood, g/dL	13.9	Male: 14-18

Question 1

A 40-year-old man presents to the emergency department with 1 episode of melena the previous night. He has not had any other symptoms. He has no other past medical therapy and takes only a multivitamin and occasional ibuprofen. On arrival, his heart rate is 75 bpm, and blood pressure is 112/70 mmHg.

His laboratory results are above.

While in the emergency department, his vitals remain stable, and he has no further episodes of melena. In addition to stopping nonsteroidal antiinflammatory drugs, what is the next best step in management?

- A. Discharge home with plan for outpatient upper endoscopy
- B. Repeat hemoglobin check in 12 hours before determining disposition plan
- C. Restrict oral intake for upper endoscopy within 24 hours
- D. Start high-dose proton pump inhibitors and follow serial hemoglobin checks

CORRECT ANSWER: A

RATIONALE

This patient has a Glasgow-Blatchford bleeding score (GBS) of 1, has a very low risk of complica-

tions, and can be safely discharged with outpatient follow-up. The GBS is a risk assessment tool to identify patients who might need transfusion or hemostatic interventions and those who are at increased risk of death. Patients with GBS of 0 to 1 are at a very low risk of complications from upper gastrointestinal bleeding and, therefore, can be safely discharged. Upper endoscopy within 24 hours would be recommended if he had a GBS higher than 1. Starting proton pump inhibitors before a procedure has only been shown to decrease the need for endoscopic interventions by downstaging ulcer stigmata and has no significant impact on other factors. Keeping the patient admitted for longer observation and blood work is unlikely to change his outcome given his very low risk and therefore is not the best option for this patient.

REFERENCE

Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG clinical guideline: upper gastrointestinal and ulcer bleeding. *Am J Gastroenterol*. 2021;116(5):899-917. doi:10.14309/ajg.0000000000001245

Question 2

A 56-year-old woman presents to the emergency department with 3 days of melena with associated weakness and dizziness upon standing. She

Laboratory Test	Result	Reference Range
Blood urea nitrogen (BUN), serum or plasma, mg/dL	65	8-20
Creatinine, serum, mg/dL	2.1	0.7-1.5
Hemoglobin, blood, g/dL	5.6	Female: 12-16

has a history of coronary artery disease and chronic obstructive pulmonary disease (COPD). She takes aspirin 81mg daily, and she recently finished a 5-day regimen of prednisone for COPD exacerbation. She reports that she recently had her annual physical examination and was told that, other than her lungs, all her other organs were “doing well.” On examination, she is noted to be mildly tachypneic, but examination is otherwise normal. Her heart rate is 117 bpm, blood pressure is 81/53 mmHg, and oxygen saturation on room air is 89%. Laboratory results are above.

She is started on a proton pump inhibitor and given 2 L of intravenous fluid and 1 unit of packed red blood cells within the first 4 hours in the emergency department. Her repeat vital signs are blood pressure, 90/61 mmHg; heart rate, 109 bpm; and oxygen saturation 97% on 2L nasal canula. Hemoglobin on recheck is 6.2 g/dL. Since arrival, she has had an additional 2 episodes of melena. What is the next best step in management of this patient’s melena?

- A. Proceed to upper endoscopy given evidence of continued upper gastrointestinal bleeding
- B. Continue to resuscitate patient until hemoglobin level is ≥7 g/dL then proceed with upper endoscopy
- C. Obtain computed tomography angiography to assess for the source of bleeding
- D. Plan to treat with proton pump inhibitor therapy for first 48 hours and observe response before pursuing endoscopy

CORRECT ANSWER: B

RATIONALE
Patients who present with upper GI bleeding should be appropriately resuscitated before upper endoscopy. Esophagogastroduodenoscopy for nonvariceal upper GI bleeding should be performed within 24 hours. Performing upper endoscopy either very early (within 6 hours) and very late (after 24 hours) has been shown to result in worse outcomes, including increased risk of intensive care unit escalation, need for repeat esophagogastroduodenoscopy, and 30-day mortality.

REFERENCES
Guo CLT, Wong SH, Lau LHS, et al. Timing of endoscopy for acute upper gastrointestinal bleeding: a territory-wide cohort study [published online ahead of print, 2021 Sep 21]. *Gut*. 2021;gutjnl-2020-323054. doi:10.1136/gutjnl-2020-323054

Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG clinical guideline: upper gastrointestinal and ulcer bleeding. *Am J Gastroenterol*. 2021;116(5):899-917. doi:10.14309/ajg.0000000000001245

Question 3
A 38-year-old man presents to the emergency department with 2 days of melena and mild epigastric pain. He has no previous medical history or significant family history but has been taking ibuprofen for the last 1 week due to ankle pain related to his training for a half-marathon. On presentation, his heart rate is 110 bpm and blood pressure is 87/52 mmHg. Laboratory results are below.

Laboratory Test	Result	Reference Range
Blood urea nitrogen (BUN), serum or plasma, mg/dL	45	8-20
Creatinine, serum, mg/dL	1.1	0.7-1.5
Hemoglobin, blood, g/dL	9	Male: 14-18

He is started on an intravenous pantoprazole 80-mg bolus followed by 8 mg/hr and given 2L of intravenous fluid with normalization of his vital signs over the next 6 hours. Which of the following outcomes would be expected to decrease with the use of proton pump inhibitor (PPI) therapy before upper endoscopy?

- A. Mortality rate
- B. Need for endoscopic intervention
- C. Length of stay
- D. Risk of future rebleeding

CORRECT ANSWER: B

RATIONALE

PPI use before endoscopy has been shown only to reduce the need for endoscopic interventions by “downgrading” ulcer stigmata. Although it has been shown to improve outcomes, such as reducing rebleeding rates when used after upper gastrointestinal ulcers are diagnosed and treated endoscopically, there is no evidence to support these benefits when used before endoscopy. Current guidelines, therefore, do not recommend for or against PPI before upper endoscopy for upper gastrointestinal bleeding unless significant delays are expected (>24 hours).

REFERENCES

Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG clinical guideline: upper gastrointestinal and ulcer bleeding. *Am J Gastroenterol.* 2021;116(5):899-917. doi:10.14309/ajg.0000000000001245

Lau JY, Leung WK, Wu JC, et al. Omeprazole before endoscopy in patients with gastrointestinal bleeding. *N Engl J Med.* 2007;356(16):1631-1640. doi:10.1056/NEJMoA065703

Question 4

A 68-year-old woman with history of rheumatic fever with distant mechanical mitral valve replacement and knee osteoarthritis was admitted 3 days

ago for melena and symptomatic anemia. Her only medication before admission was warfarin, but she also endorsed several days of ibuprofen use for knee pain. After resuscitation and optimization of her anticoagulation status, she underwent upper endoscopy with identification of a duodenal bulb ulcer with an oozing visible vessel that was treated with injection of epinephrine solution and bipolar cautery for hemostasis. She was started on intravenous pantoprazole 40 mg twice daily after the procedure and was doing well until this morning when she developed recurrent melena and a decrease in hemoglobin level from 8.5 g/dL to 7.2 g/dL overnight. What is the next step in management of her recurrent upper gastrointestinal bleeding?

- A. Stop heparin drip and monitor for improvement in bleeding
- B. Change pantoprazole from intermittent dosing to continuous infusion
- C. Obtain surgical consultation for management of recurrent ulcer bleeding
- D. Repeat esophagogastroduodenoscopy for second attempt at hemostasis

CORRECT ANSWER: D

Rationale: Repeat attempts at endoscopic therapy achieved hemostasis in approximately three-quarters of cases and had significantly lower risks when compared with surgery. Evolving data with a recent randomized controlled trial suggests that durable hemostasis rates may improve even further when over-the-scope clips (OTSC) are used compared with standard dual therapy with epinephrine and either clips or bipolar cautery (study primarily involved epinephrine/clips as comparator). Reduction in rebleeding was 15.2% (5/33) with OTSC versus 57.6% (19/33) with standard dual therapy. Patients with a mechanical mitral valve are at high risk of thrombotic events and should not have heparin stopped for prolonged periods of time. In addition, stopping heparin alone will be unlikely to stop recurrent ulcer bleeding in this patient. There is no strong evidence to sup-

port superiority of proton pump inhibitor infusion over intermittent dosing and, therefore, this would not adequately address recurrent bleeding. Surgery and/or interventional radiology consultation should be reserved until after 2 failed attempts at endoscopic hemostasis.

REFERENCES

Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG clinical guideline: upper gastrointestinal and ulcer bleeding. *Am J Gastroenterol*. 2021;116(5):899-917. doi:10.14309/ajg.0000000000001245

Schmidt A, Gölder S, Goetz M, et al. Over-the-scope clips are more effective than standard endoscopic therapy for patients with recurrent bleeding of peptic ulcers. *Gastroenterology*. 2018;155(3):674-686.e6. doi:10.1053/j.gastro.2018.05.037

Sverdén E, Mattsson F, Lindström D, Sondén A, Lu Y, Lagergren J. Transcatheter arterial embolization compared with surgery for uncontrolled peptic ulcer bleeding: A Population-based Cohort Study. *Ann Surg*. 2019;269(2):304-309. doi:10.1097/SLA.0000000000002565

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Question 5

A 78-year-old man with history of hypertension, chronic kidney disease, and coronary artery disease presents to the emergency department

with sudden-onset abdominal cramping 6 hours ago and passage of large volume hematochezia just before presentation. He takes low-dose daily aspirin, metoprolol, and lisinopril. On arrival, he is afebrile, tachycardic to 115 bpm, and his blood pressure is 96/54 mmHg. He has mild tenderness and guarding but no findings of peritonitis on examination. Stool infectious workup is negative, and additional laboratory results are below.

Computed tomography (CT) of the abdomen and pelvis was done without contrast due to his creatinine level and showed mild nonspecific inflammation of the ascending colon but no other findings. He undergoes colonoscopy, which shows multiple clean-based ulcers of various size, mucosal edema, and friability of the cecum, ascending, and proximal transverse colon. In addition to starting antibiotics and removing offending medications, what is the next step in management?

- A. CT angiography
- B. Repeat colonoscopy in 3 months to assess mucosal healing
- C. Prebiologic workup
- D. Hypercoagulable workup

CORRECT ANSWER: A

RATIONALE

This patient has isolated right colon ischemia (IRCI). IRCI should be considered a unique subcategory of colonic ischemia. It can present with abdominal pain with or without bleeding. Although bleeding occurs less commonly in IRCI than in left-sided colonic ischemia, it tends to be more severe. Patients with IRCI more commonly have atrial fibrillation, coronary artery disease, and chronic kidney disease as compared with

Laboratory Test	Result	Reference Range
Blood urea nitrogen (BUN), serum or plasma, mg/dL	19	8-20
Creatinine, serum, mg/dL	1.7	0.7-1.5
Hemoglobin, blood, g/dL	9	Male: 14-18
Leukocyte count, cells/ μ L	1600	4000-11,000
Sodium, serum, mEq/L	141	136-145

colonic ischemia affecting other segments. These patients have worse outcomes with higher 30-day mortality and more frequently require surgery. IRCI is suspected to be a “heralding” event that suggests superior mesenteric artery pathology or an impending acute mesenteric ischemia, so CT angiography should be performed before discharge to better assess the superior mesenteric artery. In addition, both IRCI and pancolonic involvement should prompt surgical evaluation. Repeat colonoscopy to assess mucosal healing is not recommended if symptoms have resolved. This patient does not have inflammatory bowel disease, so prebiologic workup would not be appropriate. Hypercoagulable workup may be appropriate if thrombosis is identified on CT angiography but is not the next best management option in this patient.

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Question 6

A 67-year-old man with history of coronary artery disease with distant history of drug-eluting stent, prior abdominal aortic aneurysm with endovascular stent repair 4 years ago, atrial fibrillation, and osteoarthritis presents to the emergency department with passage of maroon stools for 12 hours.

He has associated dizziness with position change but no hematemesis. He takes aspirin, apixaban, and occasional ibuprofen. His heart rate is 120 bpm, and blood pressure is 86/50 mmHg. Laboratory tests reveal a hemoglobin level of 9 g/dL, decreased from a previously normal baseline (reference range [male], 14-18 g/dL) and creatinine level is 0.9 mg/dL (reference range, 0.7-1.5 mg/dL). After fluid resuscitation, his blood pressure improves to 110/62 mmHg, but he remains tachycardic to 105 bpm and has an additional episode of witnessed maroon stool. He undergoes urgent upper endoscopy, which reveals a few small non-bleeding erosions in the stomach but is otherwise unremarkable to the second portion of the duodenum. What is the next best step in evaluation of his bleeding?

- A. Rapid bowel preparation then urgent colonoscopy
- B. Push enteroscopy
- C. Tagged red blood cell scan
- D. Computed tomography angiography

CORRECT ANSWER: D

RATIONALE

This patient is presenting with hemodynamically significant bleeding from an aortoenteric fistula, which is a rare but life-threatening complication after abdominal aortic aneurysm repair due to erosion of the graft and fistula formation to the gastrointestinal lumen. Fistulas most commonly involve the duodenum but can also occur in the more distal small bowel, colon, or esophagus. On initial presentation, evidence of hemodynamically significant bleeding is present and, although this patient's stool is maroon, brisk upper gastrointestinal should be ruled out first given risk factors of nonsteroidal antiinflammatory drugs use. However, the next best step for this patient, given his history of aortic aneurysm repair, is computed tomography angiography. Rapid preparation with urgent colonoscopy would be correct as the next step if he did not have this history. A tagged red blood scan and push enteroscopy can be helpful

if bidirectional endoscopy is negative in patients with a suspected small bowel source of bleeding, which might be helpful in a patient with small bowel bleeding risk factors of atrial fibrillation and nonsteroidal antiinflammatory drug use but would only delay diagnosis and/or management of this life-threatening condition.

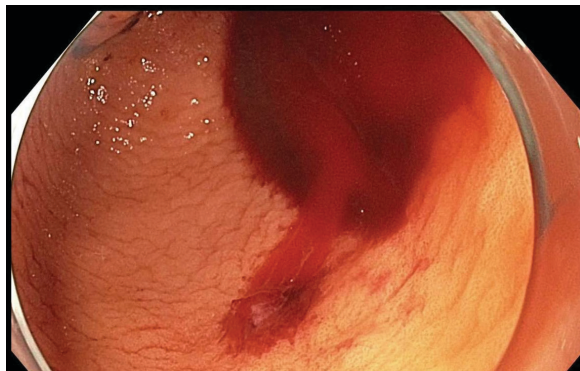
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Question 7

A 47-year-old man presents to the emergency department with sudden-onset hematemesis. He has no personal or family medical history, uses ibuprofen twice monthly but takes no prescription medications, and consumes 15 servings of alcohol weekly. On examination, his abdominal examination is unremarkable, and there is no stool in the rectal vault. His blood pressure is 96/61 mmHg and heart rate is 112 bpm. Laboratory studies reveal a hemoglobin level of 8 g/dL (reference range [male], 14-18 g/dL) down from 13 g/dL on recent annual laboratory testing. After resuscitation and initiation of intravenous proton pump inhibitor therapy, he undergoes urgent upper endoscopy with the findings below:



What is the best approach to management of this lesion?

- A. Injection of cyanoacrylate (glue) into base of the lesion and evaluate for transjugular intrahepatic portosystemic shunt
- B. Injection of epinephrine and application of through-the-scope hemostatic clips for marking
- C. Injection of epinephrine, bipolar cautery, and tattoo to mark site
- D. Application of TC-325 hemostatic spray and close observation

CORRECT ANSWER: C

RATIONALE

The lesion shown is a Dieulafoy lesion, which is an aberrant dilated submucosal artery that erodes through the mucosa. These lesions are not associated with an overlying ulceration or mass. These lesions are most commonly found in the proximal stomach, as seen in this patient, but can occur elsewhere in the gastrointestinal lumen, so suspicion should remain high in patients with unexplained large-volume gastrointestinal bleeding. Dieulafoy lesions are more common in males, in the fifth through seventh decade of life, and in patients with cardiac, respiratory, and chronic kidney diseases. Dual therapy is the ideal treatment for these lesions. No clear evidence exists yet to strongly recommend thermal therapy over mechanical therapy (through-the-scope or over-the-scope clips). Band ligation can also be used but carries increased risk of perforation when used in the proximal stomach. Regardless of the modality of treatment, the site should be tattooed to help localize the site should rebleeding occur in the future. Although cyanoacrylate injection has been described, injection monotherapy has high rates of rebleeding and complications. This modality is better used for gastric varices alone or in combination with endoscopic ultrasound-guided coils, depending on the center's expertise. Application of TC-325 spray has evolving evidence of efficacy as monotherapy for peptic ulcer bleeding but has not yet been shown to be adequate therapy for Dieulafoy lesions.

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Lee YT, Walmsley RS, Leong RW, Sung JJ. Dieulafoy's lesion. *Gastrointest Endosc*. 2003;58(2):236-43. doi:10.1067/mge.2003.328

Question 8

A 78-year-old woman presents to the emergency department with 24 hours of large-volume hematochezia and associated dizziness upon standing. She has history of coronary artery disease and is taking aspirin 81 mg. She previously took a proton pump inhibitor but stopped several months ago. She reports that a prior upper and lower endoscopy done 3 years ago was normal except for mild esophagitis and sigmoid diverticulosis. Her heart rate is 111 bpm, and her blood pressure is 104/62 mmHg. Her abdominal examination is unremarkable, but there is maroon stool and clot in the rectal vault. Her hemoglobin level is 9.2 g/dL (reference range [female], 12-16 g/dL), which is down from her baseline of 13.1 g/dL. After resuscitation, she undergoes upper endoscopy, which was normal to the second portion of the duodenum. Her repeat hemoglobin result is 9.1 g/dL, but her heart rate has improved slightly to 100 bpm, and blood pressure remains at 102/65 mmHg.

What is the next best step in management of her hematochezia?

- A. Video capsule endoscopy to better localize bleeding source
- B. Urgent colonoscopy without preparation
- C. Rapid bowel purge for colonoscopy within 24 hours
- D. Computed tomography angiography to identify source of bleeding

CORRECT ANSWER: C

RATIONALE

This patient presented with severe hematochezia with initial hemodynamic changes but has started to stabilize since admission. Emergent upper endoscopy was negative, and the next best step is colonoscopy. Early colonoscopy within 24 hours has been shown to increase diagnostic and therapeutic yield as well as shorten length of stay. However, it is essential that patients complete a bowel preparation to reduce risk of perforation and increase visibility of stigmata. Video capsule endoscopy is appropriate if colonoscopy is negative in this patient but is not the next best step. Computed tomography angiography, which will detect bleeding of 0.5 mL/minute or higher, is unlikely to identify active source of bleeding in this patient since her rate of bleeding appears to be clinically slowing.

REFERENCES

ASGE Standards of Practice Committee, Pasha SF, Shergill A, et al. The role of endoscopy in the patient with lower GI bleeding. *Gastrointest Endosc*. 2014;79(6):875-885. doi:10.1016/j.gie.2013.10.039

Strate LL, Gralnek IM. ACG clinical guideline: management of patients with acute lower gastrointestinal bleeding. *Am J Gastroenterol*. 2016;111(4):459-474. doi:10.1038/ajg.2016.41

Question 9

An 81-year-old man presents overnight to the emergency department with 24 hours of painless hematochezia. He has not had any associated symptoms or preceding illnesses. He has a history of diverticulosis found on screening colonoscopy 6 years ago, hypertension, and coronary artery disease. He takes 81 mg aspirin daily and metoprolol. On arrival, his heart rate is 70 bpm and blood pressure is 110/71 mmHg. His abdominal examination is unremarkable, but there is red blood in the rectal vault. He completes a rapid purge then proceeds to colonoscopy that morning, which shows on the following page.



What should be done next?

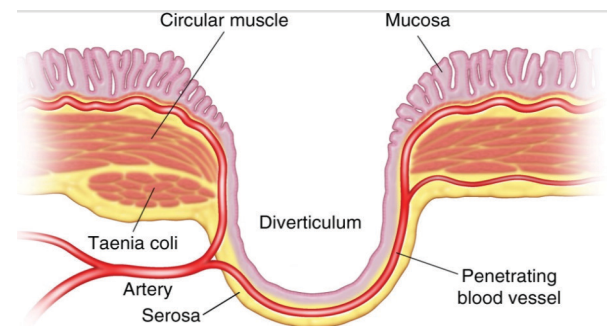
- A. No endoscopic intervention, continue to monitor hemoglobin after procedure for 24-48 hours
- B. No endoscopic intervention, tattoo near diverticulum, and obtain surgical consult for sigmoid resection
- C. Epinephrine injection and bipolar cautery to the lesion, tattoo near site after hemostasis
- D. Epinephrine injection and placement of hemostatic clips along either side of the lesion, tattoo near site after hemostasis

CORRECT ANSWER: D

RATIONALE

The endoscopic image shows a visible vessel and small area of adherent clot at the base of a diverticulum, which is best treated with dual therapy with epinephrine, hemoclips, and marking with tattoo for future localization. It is important to understand the distribution of blood supply to a diverticulum and to identify the position of the stigmata before determining the best approach to treatment. Vessels or other stigmata located deep within a diverticulum pocket are referred to as being in the base, whereas vessels positioned along luminal edge are in the neck. Stigmata in the base should be treated only with epinephrine injection plus placement of hemoclips approximately 5 mm to either side of and on top of the stigmata to occlude arterial flow. Hemoclips should be placed within the base and not along

the mucosal edges or neck due to ineffective compression of underlying artery. However, using hemoclips to zipper the diverticulum closed to tamponade the bleeding vessel can be effective in some patients. Thermal therapy should not be used for base lesions due to risk of perforation but is safe for use in neck lesions due to the location over muscle layer. Band ligation is another alternative option that can be used to treat stigmata in either the neck or base but can be technically challenging if the lesion is located in the right colon.



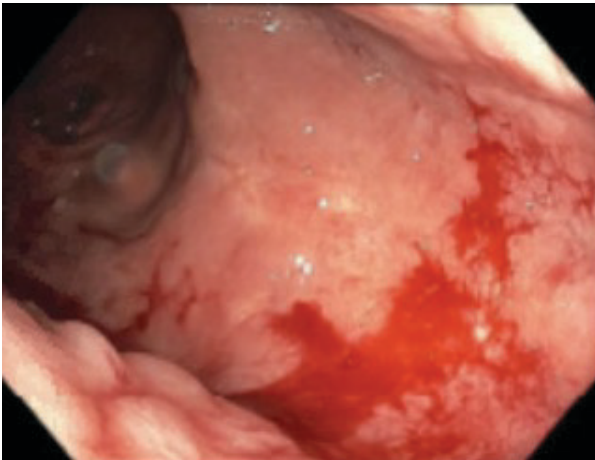
Stigmata of recent hemorrhage should be treated when found in diverticular bleeding. Patients who do not undergo endoscopic treatment have been shown to have longer length of stays, higher and more severe rebleeding, and higher rates of surgery and embolization, in part possibly because diverticular bleeding is arterial in nature. Surgical evaluation can be considered if the patient has recurrent episodes of bleeding but carries increased rates of complications over endoscopic hemostasis for the first episode of bleeding.

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Question 10

A 71-year-old man presents for outpatient colonoscopy to further evaluate intermittent small-volume painless hematochezia occurring over the last 3 months. He has had associated iron deficiency anemia and his hemoglobin level remains at 9 g/dL (reference range [male], 14–18 g/dL) despite oral iron supplementation. He has a history of prostate cancer treated with radiation 4 years ago and smokes tobacco with a 50 pack-year history but no other comorbidities. He is not taking any medications except for oral iron. He has no family history of gastrointestinal malignancies and had his last screening colonoscopy done 4 years ago that was unremarkable except for small internal hemorrhoids and mild diverticulosis. He undergoes colonoscopy with excellent preparation (Boston Bowel Preparation Scale = 9) and is found to have only sigmoid diverticulosis. On withdrawal into the rectum, the following is seen:



What is the next best step in therapy?

- A. Subcutaneous octreotide 100 mcg three times daily
- B. Argon plasma coagulation
- C. Biopsy with immunohistochemical stain
- D. Formalin application to rectal mucosa

CORRECT ANSWER: B

RATIONALE

This patient has chronic radiation proctitis with

oozing leading to persistent iron deficiency anemia despite oral supplementation. Chronic radiation proctitis is related to mucosal injury from radiation therapy, resulting in mucosal friability, ulcers, fistula, and telangiectasias starting as early as 3 months after radiation to pelvic organs but can occur years later. Medical therapy is typically first-line therapy for mild symptoms and includes sucralfate enemas. Short-chain fatty acid enemas have been shown to be helpful in acute radiation proctitis but show little benefit in chronic presentations. Products containing 5-aminosalicylic acid also have limited benefit in this condition. When symptoms are more severe, endoscopic therapy with argon plasma coagulation is best, as is the case with this patient. Subcutaneous octreotide has been described for management of gastrointestinal angioectasias but has no role in radiation proctitis. Biopsies should be avoided in this condition due to risk of fistula formation. Direct application of formalin is an accepted treatment for chronic radiation proctitis but carries higher risks including stricture formation and is not preferred as first-line therapy.

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Question 11

A 75-year-old man is admitted to the hospital for intermittent melena over the last 2 weeks. He has no prior cardiac history but is taking aspirin for primary prophylaxis and takes ibuprofen occasionally for shoulder osteoarthritis pain. His hemoglobin level on presentation is 10 g/dL (reference range [male], 14–18 g/dL). He is started on a proton pump inhibitor and within 24 hours undergoes upper endoscopy, which reveals a 1-cm duodenal bulb ulcer with clean-ulcer base (Forrest

class III) that did not require treatment. *Helicobacter pylori* testing is negative.

What is your recommendation for this patient?

- A. Start oral pantoprazole 40 mg twice daily
- B. Resume aspirin 81 mg but avoid other non-steroidal antiinflammatory drugs (NSAIDs)
- C. Avoid all NSAIDs, including aspirin 81 mg, going forward
- D. Repeat upper endoscopy in 8 weeks to assess healing

CORRECT ANSWER: C

RATIONALE

This patient was taking aspirin for primary prophylaxis. Both the US Preventive Services Task Force and joint American College of Cardiology/American Heart Association guidelines recommend use of primary aspirin prophylaxis for individuals 40 to 70 years of age and who are not at increased risk of gastrointestinal bleeding. This patient is older than 70 years of age and has demonstrated ulcer bleeding secondary to NSAID use, so he should not resume aspirin. Given that he has a clean-based ulcer, a once-daily oral proton pump inhibitor is adequate therapy. Gastric, not duodenal, ulcers require repeat upper endoscopy to assess healing given their risk of underlying malignancy.

REFERENCES

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Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG clinical guideline: upper gastrointestinal and ulcer bleeding. *Am J Gastroenterol*. 2021;116(5):899-917. doi:10.14309/ajg.0000000000001245

Question 12

A 40-year-old woman with class II obesity presents to the emergency department with constant gnawing epigastric pain unrelated to food, intermittent melena, and fatigue over the last 2 weeks. She has history of an uncomplicated Roux-en-Y gastric bypass 1 year ago with resulting 80-lb weight loss. She takes no medications except for acetaminophen as needed for back pain. She does not drink alcohol or use nonsteroidal antiinflammatory drugs but does smoke tobacco products. On examination, she has evidence of laparoscopic scars without associated sensory changes, and carnet sign is negative. Laboratory results are below.

She undergoes an upper endoscopy and is found to have expected postsurgical anatomy without strictures or fistulas but with a 2-cm marginal ulcer with flat-pigmented material along the jejunal aspect of the gastrojejunal anastomosis. *Helicobacter pylori* testing is negative. In addition to an open-capsule proton pump inhibitor and iron supplementation, what other recommendation should be made?

- A. Follow-up with bariatric surgeon for revision of gastrojejunal anastomosis
- B. Repeat upper endoscopy in 4 weeks to assess healing
- C. Offer tobacco cessation counseling services
- D. Order right upper quadrant ultrasound

CORRECT ANSWER: C

Laboratory Test	Result	Reference Range
Ferritin, serum, ng/mL	7	Female: 24-307
Hemoglobin, blood, g/dL	8.1 (3 months ago, 12.3)	Female: 12-16
Mean corpuscular volume, fL	71	80-98

Laboratory Test	Result	Reference Range
Hemoglobin, blood, g/dL	7.1 (baseline, 14)	Male: 14–18
International normalized ratio	1.0	<1.1
Platelet count, <i>plt</i> / μ L	230,000	150,000–450,000

RATIONALE

Patients with Roux-en-Y gastric bypasses are at risk of marginal ulcers, which is what is causing this patient's abdominal pain, melena, and iron-deficiency anemia. Marginal ulcers typically occur on the jejunal-side of gastrojejunal anastomosis due to the jejunum's inability to tolerate acid exposure. Local ischemia is also a significant contributor to formation of marginal ulcers. This patient smokes tobacco, which is her main risk factor for marginal ulcer. Therefore, in addition to treating with a soluble or open-capsule proton pump inhibitor to heal the ulcer, she should work to stop smoking to prevent recurrent or nonhealing ulcers in the future. Referral to bariatric surgery would be appropriate if her ulcer continues to persist and cause symptoms despite appropriate medical management and risk factor reduction. Since ulcers are on the jejunal aspect of marginal ulcers, routine repeat upper endoscopy is not necessary if symptoms resolve. In addition, 4 weeks would be too premature to assess healing. Patients with Roux-en-Y gastric bypass can develop gallstone disease as the cause of upper abdominal pain. However, her symptoms are not biliary in nature, and her abdominal pain is related to her ulcer as is commonly described in patients with Roux-en-Y gastric bypasses.

REFERENCE

Schulman AR, Thompson CC. Abdominal pain in the Roux-en-Y gastric bypass patient. *Am J Gastroenterol*. 2018;113(2):161-166. doi:10.1038/ajg.2017.361

Question 13

A 72-year-old man presents with multiple episodes of passage of frank red blood per rectum over last 6 hours. He has history of prior non-ST-elevation myocardial infarction with drug-

eluting stent 2 years ago on aspirin monotherapy. He is weak, dizzy with position change but denies abdominal pain or emesis. He has never had prior gastrointestinal (GI) bleeding in the past. He had a colonoscopy 3 years ago with diverticulosis and a 2.5 cm tubular adenoma that was resected piecemeal, and he admits he is overdue for surveillance. On examination he is diaphoretic and pale and has a soft, nontender abdomen. There is maroon stool with clot in the rectal vault. Heart rate is 125 bpm and blood pressure is 75/43 mmHg. Laboratory results are above.

The patient's hemodynamics stabilize after resuscitation with intravenous fluids and 3 units packed red blood cells over the next few hours. What is the next best step in management?

- A. Proceed to emergent colonoscopy without preparation
- B. Rapid bowel purge with 4 L of polyethylene glycol and colonoscopy within next 12-24 hours
- C. Computed tomography angiography to better localize bleeding source
- D. Urgent upper endoscopy

CORRECT ANSWER: D

RATIONALE

Patients presenting with severe hematochezia with associated hemodynamic instability should have the brisk upper GI source of bleeding excluded first with urgent esophagogastroduodenoscopy once they are stabilized. This patient has risk factors for upper GI bleeding from aspirin ingestion and is presenting with brisk peptic ulcer hemorrhage. Proceeding without preparation for the colonoscopy will increase the patient's risk of complications including perforation, decrease likelihood of finding stigmata

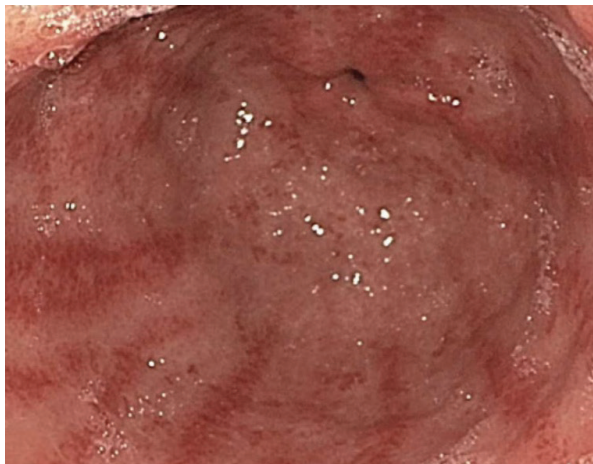
given poor visibility, and delay diagnosis of brisk upper GI source of bleeding. Delaying upper GI evaluation to complete a rapid preparation also risks delay in diagnosis. Computed tomography angiography can detect bleeding at a rate of 0.5 mL/minute but can miss identification of the source, particularly if the patient is having bleeding from a gastric ulcer and the stomach is already full of blood and would only further delay evaluation of brisk upper GI hemorrhage.

REFERENCE

Strate LL, Gralnek IM. ACG clinical guideline: management of patients with acute lower gastrointestinal bleeding. *Am J Gastroenterol*. 2016;111(4):459-474. doi:10.1038/ajg.2016.41

Question 14

A 72-year-old woman presents for outpatient upper endoscopy and colonoscopy to evaluate progressive iron-deficiency anemia and intermittent dark stools over the last 2 months. She has a history of hypertension, which is treated with lisinopril, and she denies use of nonsteroidal antiinflammatory drugs. She has had previous screening colonoscopies but has never had upper endoscopy. On esophagogastroduodenoscopy, you see the following:



What physical examination finding would you also expect to find?

- A. Thickened, tight skin of the fingers
- B. Telangiectasias of the buccal membranes
- C. Mid-systolic ejection murmur
- D. Red, swollen nodules over the shins

CORRECT ANSWER: A

RATIONALE

This patient has gastric antral vascular ectasias (GAVE), which is shown in the endoscopic image as linear streaking antral erythema. This is associated with a number of conditions, including systemic sclerosis, which leads to sclerodactyly, or thickened, tight skin of the fingers. Other conditions associated with GAVE include cirrhosis, systemic lupus erythematosus, CREST (calcinosis, Raynaud, esophageal dysmotility, scleroderma, telangiectasia) syndrome, Raynaud syndrome, Sjogren syndrome, polymyalgia rheumatica, chronic kidney disease, diabetes mellitus, coronary artery disease, Parkinson disease, monoclonal gammopathy of undetermined significance, acute myelogenous leukemia, and prior bone marrow transplantation.

Telangiectasias of the buccal membranes and associated angiodyplasias or angioectasias is seen in hereditary hemorrhagic telangiectasia. A mid-systolic ejection murmur is found in aortic stenosis, which is associated with the Heyde syndrome triad of aortic stenosis, acquired von Willebrand syndrome, and intestinal angiodysplasias. Red, swollen nodules over the shins are consistent with erythema nodosum, which is seen in inflammatory bowel disease and Behcet disease, which can also cause anemia and gastrointestinal bleeding but does not have direct association with GAVE.

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Wang J, Stine JG, Cornella SL, Argo CK, Cohn SM. Patients with gastric antral vascular ectasia

Laboratory Test	Result	Reference Range
Hemoglobin, blood, g/dL	9.1	Male: 14–18
International normalized ratio	0.9	<1.1
Platelet count, <i>plt</i> / μ L	250,000	150,000–450,000

(GAVE) are at a higher risk of gastrointestinal bleeding in the absence of cirrhosis. *J Clin Transl Hepatol.* 2015;28;3(4):254–9. doi:10.14218/JCTH.2015.00031

Question 15

A 23-year-old man is admitted to the hospital for hematochezia. He has no past medical history, has no significant family history, and takes no medication. He reports his hematochezia started 24 hours ago and that he has had several bowel movements that filled the toilet with blood. On examination, he is in no distress, but his heart rate is 105 bpm and blood pressure is 99/57 mmHg. Laboratory results are above.

He initially undergoes upper endoscopy and colonoscopy within the first 24 hours, which are normal, except for trace blood in the terminal ileum. He subsequently undergoes video capsule endoscopy and computed tomography enterography within the next 24 hours, which are normal. His hemoglobin level on recheck is 9.2 g/dL.

What is the next best step in management?

- A. Refer for provocative angiography
- B. Obtain technetium-99m–labeled red blood cell scan
- C. Perform push enteroscopy
- D. Obtain technetium-99m pertechnetate scan

CORRECT ANSWER: A

RATIONALE

This patient has a Meckel diverticulum leading to self-limited significant hematochezia. Although Meckel diverticulum is typically a congenital anomaly discovered during childhood, symptoms can develop in adulthood as well. Patients are typically males under the age of 50 years who

present with bleeding, which can vary in severity from mild intermittent bleeding to hemodynamically significant hematochezia. Meckel diverticulum typically contains ectopic gastric mucosa, which secrete acid that leads to ulceration of surrounding ileal mucosa; however, less commonly, the diverticulum may also contain ectopic pancreatic tissue. Meckel diverticula are commonly missed on imaging studies including angiography, and thus high suspicion should be maintained for younger patients who present with hematochezia. Provocative angiography can be considered in cases where no bleeding source can be identified and all other diagnostic studies have been exhausted. A technetium-99m–labeled red blood cell scan can detect bleeding rates as low as 0.1 mL/min and can be helpful in questions of small bowel bleeding but will be negative as this patient has stopped bleeding, as evidenced by stable hemoglobin after more than 24 hours. Repeat push enteroscopy is appropriate when evaluating for a suspected small bowel source. However, given risk of missed lesions, it would not be helpful in this patient.

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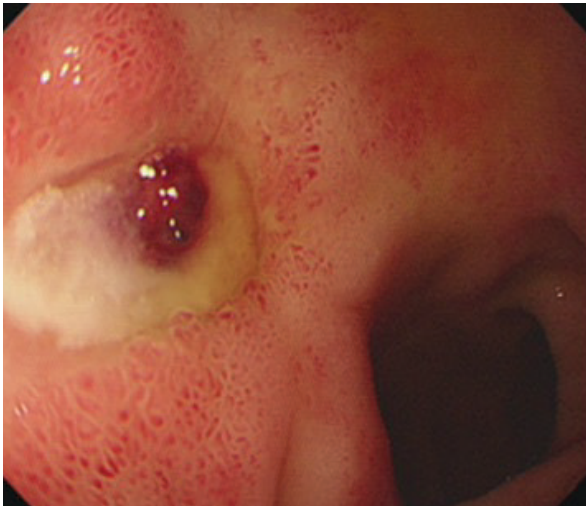
Spottswood SE, Pfluger T, Bartold SP, et al. Society of Nuclear Medicine and Molecular Imaging; European Association of Nuclear Medicine. SNMMI and EANM practice guideline for meckel diverticulum scintigraphy 2.0. *J Nucl Med Technol.* 2014;42(3):163–9. doi:10.2967/jnmt.113.136242

Laboratory Test	Result	Reference Range
Hemoglobin, blood, g/dL	8.1 (baseline, normal)	Male: 14–18
International normalized ratio	1	<1.1
Platelet count, plt/ μ L	240,000	150,000–450,000

Question 16

A 46-year-old man presents to the emergency department with melena for the last 2 days. He has history of chronic back pain and takes ibuprofen 3 times weekly. On presentation, his vital signs are stable. His abdominal examination is soft and nontender, and melena is present on rectal examination. Laboratory results are above.

He undergoes upper endoscopy, and the following is seen in the duodenum:



Which of the following is the most appropriate next step in management?

- A. No endoscopic therapy, start twice-daily proton pump inhibitor
- B. Inject 1:20,000 epinephrine solution for hemostasis
- C. Inject 1:10,000 epinephrine solution and use bipolar cautery to lesion
- D. Treat with TC-325 hemostatic powder
- E. Consult interventional radiology for embolization

CORRECT ANSWER: C

RATIONALE

The above image shows a duodenal ulcer with visible vessel and small neighboring adherent clot. This lesion carries up to a 50% risk of recurrent bleeding when treated with medical therapy alone and therefore should be treated with endoscopic therapy. Epinephrine monotherapy is not adequate for durable hemostasis, so dual therapy with epinephrine plus either therapy or hemostatic clips should be used. Evolving evidence suggests that use of TC-325 hemostatic spray may be an effective monotherapy for nonvariceal upper gastrointestinal bleeding. However, lesions must be actively bleeding for this modality to be effective, so it would be ineffective in this patient. Interventional radiology would be an appropriate option for bleeding that cannot be controlled endoscopically or recurrent bleeding after second attempt at endoscopic hemostasis but would not be appropriate in this patient.

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Question 17

A 67-year-old man is admitted to the hospital with 24 hours of melena. He has history of hypertension and chronic kidney disease, and his only medication is lisinopril. On examination, he is hemodynamically stable with unremarkable abdominal examination but evidence of melena on rectal examination. His hemoglobin level is 9 g/dL (baseline, 10.8 g/dL; reference range [male], 14–18 g/dL). He successfully undergoes upper endoscopy where a 2-cm ulcer with flat-pigmented material is found in the gastric body. *Helicobacter pylori* testing is negative. After the procedure, he asks what the risk is for recurrent bleeding.

What do you tell him?

- A. 5%
- B. 10%
- C. 22%
- D. 43%
- E. 55%

CORRECT ANSWER: B

RATIONALE

The risk of recurrent bleeding from an ulcer with flat-pigmented material, or spots, in the absence of other risk factors is approximately 10%. The risk of rebleeding from a clean-based ulcer is 5%. Ulcers that have stigmata carry higher risk of rebleeding. Ulcers with an adherent clot have a 22% risk of rebleeding, nonbleeding visible vessels have a 43% chance of rebleeding, and actively bleeding lesions have a 55% risk of recurrent bleeding without endoscopic therapy.

REFERENCE

Laine L, Peterson WL. Bleeding Peptic Ulcer. *New England Journal of Medicine.*

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Question 18

A 61-year-old woman presents to the emergency department with 3 days of intermittent melena. She has a history of well-controlled diabetes mellitus and hypertension and takes metformin and lisinopril. On examination, her blood pressure is 121/76 mmHg and heart rate is 75 bpm. Her abdomen is soft and nontender, and there is no stool on rectal examination. She undergoes upper endoscopy and is found to have a 1-cm clean-based ulcer in the duodenal bulb.

What should you recommend as next steps in management?

- A. Discharge home with oral proton pump inhibitor (PPI)
- B. Start oral PPI and monitor for 24 hours to check serial hemoglobin levels
- C. Administer PPI intravenously twice daily for 72 hours
- D. Consult interventional radiology for empiric embolization

CORRECT ANSWER: A

RATIONALE

This patient has a Forrest III (clean-based) duodenal ulcer, which carries a less than 5% chance of recurrent bleeding, is hemodynamically stable, and is not high risk. Early discharge was shown in a randomized controlled trial to be safe and cost-effective in this patient population.

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Question 19

A 62-year-old man is admitted with intermittent melena over the last 1 month with associated fatigue, anorexia, and a 10-pound unintentional weight loss. He has history of atrial fibrillation, for which he takes apixaban, and is a current smoker with a 50 pack-year history. On examination, his vitals are within normal limits, and his abdominal examination is unremarkable. On rectal examination, melena is noted. Laboratory results reveal hemoglobin level of 8 g/dL (reference range [male], 14-18 g/dL), and he is found to be iron deficient. His apixaban is held, and he undergoes esophagogastroduodenoscopy (EGD) and colonoscopy with intubation of the terminal ileum, both of which are normal. The preparation was noted to be excellent, and there was no blood seen. A video capsule endoscopy (VCE) is subsequently performed and is also negative. What is the next best step in management?

- A. Computed tomography (CT) angiography
- B. Push enteroscopy
- C. CT enterography
- D. Interventional radiology consultation for provocative angiography

CORRECT ANSWER: C

RATIONALE

This patient is presenting with overt gastrointestinal (GI) bleeding from a suspected small bowel source with associated malignancy-related symptoms. Although small intestine adenocarcinoma accounts for only around 2% of GI cancers, it should be considered in patients who present with evidence of GI bleeding and have negative EGD, colonoscopy, and VCE. CT enterography is the next best step in evaluation. It uses neutral contrast to highlight hyper-enhancing lesions or bleeding and can also evaluate for submucosal pathology. CT enterography has been shown to be superior to VCE in detecting small bowel masses and can increase diagnostic yield by 40% to 50% in patients with negative EGD, colonoscopy, and VCE. CT angiography is useful in patients with

active bleeding but can miss small bowel masses. Performing push enteroscopy in a patient with overt upper GI bleeding from a suspected small bowel source is the recommended next step in patients who undergo EGD, colonoscopy, and VCE, given risk of missed lesions on EGD and VCE in the duodenum. Use of provocative angiography is reserved for suspected small bowel source of bleeding when all other testing is negative.

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Huprich JE, Fletcher JG, Fidler JL, et al. Prospective blinded comparison of wireless capsule endoscopy and multiphase CT enterography in obscure gastrointestinal bleeding. *Radiology*. 2011;260(3):744-51. doi:10.1148/radiol.11110143

Question 20

A 72-year-old woman is admitted with reports of episodes of dark stool and progressive fatigue for the last 5 weeks. She has been craving ice but otherwise has no other symptoms. She has history of end-stage renal disease treated with hemodialysis and had some “abdominal surgery” as a child; she has had 2 admissions in the last 3 years for small bowel obstructions. On examination, her blood pressure is 112/67 mmHg, and her heart rate is 70 bpm. Her abdominal examination is normal, with no stool on rectal examination. Her hemoglobin is initially 6.4 g/dL (reference range [female], 12-16 g/dL) from a baseline of 9.4 g/dL, and she is iron deficient. She receives 1 unit of packed red blood cell transfusion and undergoes esophagogastroduodenoscopy (EGD) and colonoscopy with

intubation of the terminal ileum, both of which are normal. Repeat hemoglobin level is 7.4 g/dL.

What is the best next step in management for this patient?

- A. 24-hour observation with serial hemoglobin tests
- B. Computed tomography enterography
- C. Video capsule endoscopy
- D. Tagged red blood cell scintigraphy

CORRECT ANSWER: B

RATIONALE

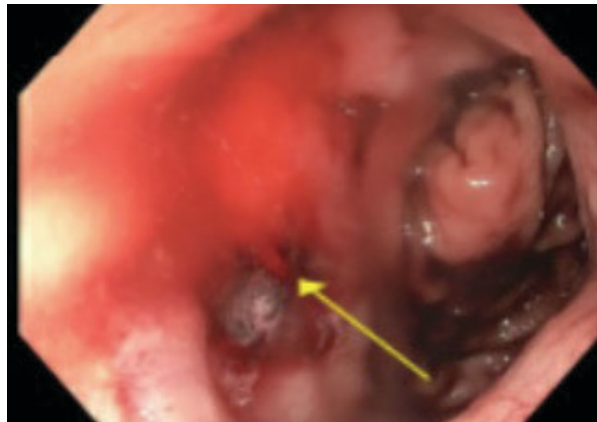
This patient has evidence of overt gastrointestinal bleeding with no source found on EGD and colonoscopy. Given this patient's age and comorbidities of end-stage renal disease, a small bowel source should be suspected. The next best option in this case is computed tomography enterography due to her history of small bowel obstruction and prior unknown abdominal surgery. Small bowel obstructions or known strictures from Crohn's disease, nonsteroidal antiinflammatory drug use, or other pathology are the most common causes of retained capsule and should prompt further imaging with computed tomography enterography, magnetic resonance enterography, or use of patency capsule before use. Observation alone would be insufficient to evaluate her substantial hemoglobin drop and melena. Tagged red blood cell scintigraphy detects bleeding at a rate of 0.1 to 0.2 mL/min and can be useful for lower-volume bleeding missed on a computed tomography angiography but has many limitations including limited ability to characterize source of bleeding and poor spatial resolution.

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Question 21

An 82-year-old woman with history of hypertension, diabetes, and chronic kidney disease develops several hours of hematochezia. She was admitted to the intensive care unit 2 days ago for sepsis secondary to urinary source. On initial computed tomography, she was found to have large stool burden in the rectum and a sigmoid colon for which she has been receiving osmotic laxatives with good effect. She responded well to initial antibiotics and was clinically improving until the hematochezia developed. On examination, her heart rate is 116 bpm, and blood pressure is 76/49 mmHg. Her abdomen is soft and nontender; red blood and clot are noted on rectal examination. She is resuscitated, and an endoscopy is performed. The upper endoscopy is negative for a brisk upper gastrointestinal source. Flexible sigmoidoscopy is next performed, revealing 5 ulcers of varying size in the rectum. In addition, an ulcer with active oozing from a visible vessel (see below) is found, and hemostasis is achieved with dual endoscopic therapy. The sigmoid and distal descending colon appear normal.



What is the most likely cause of this patient's bleeding?

- A. Ischemic proctitis
- B. Cytomegalovirus proctitis
- C. Acute hemorrhagic rectal ulcer
- D. Dieulafoy lesion

CORRECT ANSWER: C

RATIONALE

The patient has developed hemodynamically significant bleeding from an acute hemorrhagic rectal ulcer. This syndrome is most commonly seen in intensive care unit patients with comorbidities, including stroke, diabetes, and history of constipation, low albumin level, and poor functional status. These ulcers can be circumferential or discrete and can have massive bleeding, as in this case. Although endoscopy is recommended, these ulcers carry a rate of rebleeding as high as 24%, despite endoscopic therapy. Ischemic proctitis is uncommon. Colonic ischemia typically affects watershed areas or areas of the colon with limited arterial blood flow, such as splenic and hepatic flexures. Although they can occur anywhere, especially in states of global hypoperfusion, occurrence in the rectum is relatively uncommon due to the dual blood supply that perfuses the area. Cytomegalovirus proctitis can result in multiple ulcers, which can bleed. However, this patient does not have risk factors for CMV proctitis, and there are other more likely etiologies. Dieulafoy lesions can occur anywhere throughout the gastrointestinal tract, but they are most common in the stomach and proximal small bowel. These lesions are not associated with underlying ulceration and would therefore be excluded in this patient.

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Question 22

A 71-year-old man is brought to the emergency department by ambulance for large volume he-

matemesis. He has a history of coronary artery disease for which he takes aspirin 81 mg daily. On examination, his heart rate is 117 bpm, and his blood pressure is 75/47 mmHg. He is confused and is noted to have dried blood around his mouth, but abdominal examination is unremarkable. His hemoglobin level is 7.1 g/dL (reference range [male], 14–18 g/dL), down from 13.5 g/dL 1 month ago. He is intubated and given a proton pump inhibitor. In anticipation of esophagogastroduodenoscopy (EGD), erythromycin 250 mg is given intravenously 30 minutes before the procedure. What is the benefit of using erythromycin before EGD for upper gastrointestinal bleeding?

- A. Improvement in EGD-related complications
- B. Reduction in rebleeding rate
- C. Decrease in patient mortality
- D. Improvement in endoscopic visualization

CORRECT ANSWER: D

RATIONALE

This patient is presenting with significant upper gastrointestinal bleeding and is likely to have a large amount of blood and clot obscuring the stomach at the time of endoscopy. The strongest evidence for the use of the prokinetic erythromycin showed increased visualization at the time of endoscopy, which lead to shortened procedure times; reduced need for repeat, or relook, endoscopy due to poor visualization; and reduced length of stay. There is little evidence that the use of preprocedure erythromycin improves outcomes such as rebleeding, procedure complications, or mortality.

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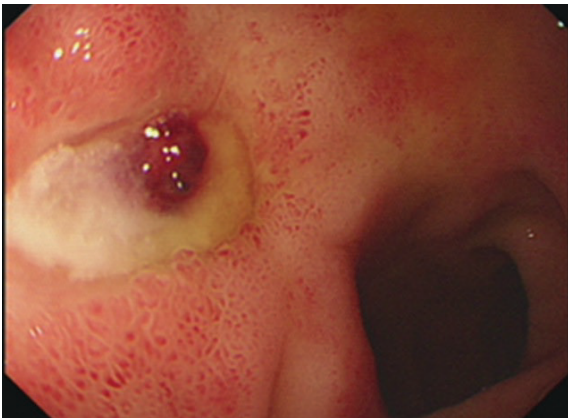
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Question 23

A 34-year-old female travel writer presents to the clinic for hospital follow-up. She has no medical history and takes only medication for seasonal allergies and naproxen several times a week. She was admitted 2 weeks ago with melena and acute anemia with a drop in hemoglobin level to 9 g/dL (reference range [female], 12-16 g/dL). She underwent urgent esophagogastroduodenoscopy with the findings shown below in the duodenum.



Biopsies taken during the hospital showed *Helicobacter pylori* (*H pylori*) infection and she was discharged on treatment with instructions to stop nonsteroidal antiinflammatory drugs (NSAIDs). Since discharge, she is feeling well, and her hemoglobin level is now 11 g/dL. She asks for guidance on her proton pump inhibitor (PPI) regimen after *H pylori* treatment is completed.

What do you tell her?

- A. Do not continue PPI
- B. Continue PPI until *H pylori* eradication confirmed
- C. Continue PPI for 8-week course
- D. Continue PPI indefinitely

CORRECT ANSWER: B

RATIONALE

The cause of this patient's ulcer with stigmata of recent bleeding is an *H pylori* infection in addition to NSAID use. She has discontinued NSAIDs, and her *H pylori* has been treated. Once *H pylori* eradication is confirmed, she can stop her PPI since eradication of *H pylori* alone is adequate to heal her ulcer as long as she continues to avoid NSAIDs. She should not stop her PPI until *H pylori* eradication is confirmed because infection serves as an independent risk factor for rebleeding. Although regimens of PPI therapy for 6 to 8 weeks are often used for treatment of ulcers requiring endoscopic therapy, as in this case, it is not necessary once *H pylori* is eradicated.

REFERENCE

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Question 24

A 70-year-old woman is admitted with 4 days of melena and fatigue. She has history of atrial fibrillation for which she takes apixaban. On initial examination, she has stable vital signs and a normal abdominal examination with trace melena on rectal examination. Her hemoglobin is 9 g/dL (reference range [female], 12-16 g/dL), which is down from recent baseline of 11.5 g/dL. She is optimized overnight, and repeat hemoglobin is 8.7 g/dL. Esophagogastroduodenoscopy is performed, revealing a 1-cm posterior wall duodenal ulcer with adherent clot. This is vigorously irrigated. However, due to positioning, the clot cannot be safely dislodged. She continues receiving a proton pump inhibitor intravenously after the procedure.

What is the best recommendation regarding her anticoagulation?

- A. Start heparin drip for 24 hours
- B. Resume home apixaban immediately
- C. Resume home apixaban before discharge in 3 days
- D. Change to dabigatran before discharge in 3 days

CORRECT ANSWER: C

RATIONALE

This patient presented with upper gastrointestinal bleeding from a duodenal ulcer with adherent clot (Forrest IIb). In this case, the clot could not be dislodged with irrigation. Although the guillotine method can be used to snare off the clot and expose an underlying lesion for treatment, this was not possible due to the position of her ulcer. Therefore, durable hemostasis was not achieved. Without intervention, her Forrest IIb ulcer carries an approximate 20% to 30% chance of rebleeding with medical therapy alone, with the highest risk within the first 72 hours. Risk of rebleeding should, however, be balanced with the risk of a thromboembolic event. This patient has a CHADS-VASc (congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke-vascular disease, age between 65-74 years, and female sex) score of 2 and has not had any major complication such as strokes in the past. Her overall risk is moderate to high for future thromboembolic events, but her day-to-day or immediate risk remains relatively low when compared with her risk of rebleeding from a Forrest IIb lesion within the early postprocedure period. The risk changes after anticoagulation is interrupted for more than 5 to 7 days and thromboembolic event rate significantly increases. Therefore, anticoagulation should be interrupted no longer than 5 to 7 days regardless of Forrest classification.

Use of heparin drip can be considered in patients with high risk of thromboembolic event such as those with mechanical valves, atrial fibrillation with prior strokes, or significant pulmonary embolus. The benefit is that it is short acting and can be stopped with quick resolution of effect if

significant bleeding does occur. This patient's indication of atrial fibrillation without complication does not warrant immediate initiation of anticoagulation. Resumption of apixaban immediately postprocedure is not the best option for this patient. Although it is short acting, it still takes 24 to 48 hours to clear in patients with normal renal function and will make management more challenging should rebleeding occur. Dabigatran has the highest risk of gastrointestinal bleeding of the direct oral anticoagulants. Continued use of apixaban, which has the lowest risk of gastrointestinal bleeding, is preferred.

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Question 25

A 72-year-old man is admitted to the hospital for symptomatic anemia for 1 month. He has not had melena or hematochezia and has no other symptoms except those from anemia including pagophagia over the last 3 weeks. He has a history of severe aortic stenosis, coronary artery disease, and gastroesophageal reflux disease, which was evaluated 2 months ago by esophagogastroduodenoscopy (EGD) and found to be normal. His medications are aspirin 81 mg and pantoprazole 40 mg daily. On evaluation, his vital signs and

examination are normal including rectal examination with trace brown stool. His hemoglobin is 8.1 g/dL (reference range [male], 14-18 g/dL) from a normal baseline 4 months ago, and he is iron deficient. Because of his recent upper endoscopy, he undergoes push enteroscopy in addition to colonoscopy to the terminal ileum. Colonoscopy preparation was excellent and both examinations are normal. His repeat hemoglobin level was 8.0 g/dL. What is the next best step in management?

- A. Discharge home with clinic follow-up in 2 weeks
- B. Video capsule endoscopy
- C. Repeat push enteroscopy
- D. Nuclear red blood cell scan

CORRECT ANSWER: B

RATIONALE

This patient is presenting with symptomatic iron-deficiency anemia from suspected small bowel, formerly “occult”, bleeding. He has now had high-quality push enteroscopy and colonoscopy with intubation of the terminal ileum, as well as an EGD 2 months prior. The next best step is to evaluate the small intestine with a video capsule endoscopy (VCE). His history of aortic stenosis puts this patient at risk of Heyde syndrome, which includes a triad of aortic stenosis, small bowel angiodysplasias, and acquired von Willebrand disorder. VCE is the preferred test for evaluating vascular abnormalities of the small bowel. Yield is highest if used quickly after presentation for either overt or suspected small bowel bleeding, with yield dropping significantly if done after 2 weeks. Therefore, although this patient now has stable hemoglobin, a plan to discharge him home with 2-week follow-up is incorrect because the delay in VCE would decrease yield of workup.

Repeat, or second look, upper or lower endoscopy is recommended most strongly in patients with overt gastrointestinal (GI) bleeding who have had high-quality EGD and colonoscopy within 2 to

3 months of presentation due to the high rate of missed lesions such as angiodysplasias. Selection of procedure should be based on localizing signs of bleeding. Push enteroscopy is the preferred procedure for repeat evaluation of the upper GI tract to best evaluate the entire duodenum and proximal jejunum. If colonoscopy is repeated, the terminal ileum should be intubated to exclude blood draining from the more proximal small bowel. Repeat procedure in this patient would not be the best option when he is having suspected small bowel bleeding and has already had push enteroscopy and colonoscopy. A nuclear-tagged red blood cell scan can detect slow GI bleeding at a rate of 0.1 mL/min but has poor localization and limited ability for characterization of lesions and, thus, is not recommended in this patient.

REFERENCE

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Question 26

An 80-year-old woman with a past medical history significant for decompensated heart failure, stroke, and severe chronic obstructive pulmonary disease receiving home oxygen presents to the emergency department with painless hematochezia. Her medication list includes aspirin 81 mg daily. Her blood pressure on arrival is 70/30 mmHg, and her heart rate is 118 bpm. Her hemoglobin is 6.1 g/dL (reference range [female], 12-16 g/dL). She appears pale and somnolent. She is given 2 units of packed red blood cells. Her blood pressure improves to 102/58 mmHg and a subsequent urgent upper endoscopy shows a gastric ulcer with an adherent clot, which is endoscopically treated. After the procedure, she develops respiratory distress, which requires intubation. She passes away on hospital day 32.

What factors would most accurately predict an increased risk of mortality in this patient?

- A. Age and comorbid status
- B. Ongoing aspirin use
- C. Presence of hematochezia over melena
- D. Use of blood products to treat anemia

CORRECT ANSWER: A

RATIONALE

Despite advances in hospital care, endoscopic and pharmacologic therapy, mortality from peptic ulcer disease is still 5% to 10% worldwide. Advancing age and comorbid status likely accounts for most of the deaths in this population. For example, in a large study from Hong Kong, there were significantly more patients who died of non-ulcer bleeding causes (79.9%) than bleeding-related causes (18.4%). Among those who died of nonbleeding-related causes, multiorgan failure (23.9%), pulmonary conditions (23.5%), and terminal malignancy (33.7%) were most common.

Although aspirin use is related to development of peptic ulcer disease, it has not shown to worsen mortality. Hematochezia in upper gastrointestinal bleeding may suggest more severe bleeding; however, in this patient, bleeding was adequately treated, and it had stopped. The patient was anemic upon arrival and has known cardiovascular disease. Although the need for transfusion does suggest significant bleeding, 2 units of packed red blood cells does not clearly correlate with increased mortality.

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Question 27

A 70-year-old man with a past medical history significant for osteoarthritis of the knees presents to his primary care physician's office with complaints of worsened pain in his knees. His physician is inclined to prescribe him a standard dose of nonsteroidal anti-inflammatory drugs (NSAID) but is contemplating which to choose to minimize his risk of upper gastrointestinal complications.

Which of the following would be most appropriate?

- A. Celecoxib
- B. Ibuprofen
- C. Ketorolac
- D. Naproxen

CORRECT ANSWER A

RATIONALE

NSAIDs are among the most widely used drugs in the world and are chiefly used to treat pain. Their long-term use is often limited by serious gastrointestinal side effects. NSAIDs inhibit the 2 recognized forms of prostaglandin G/H synthase (also referred to as COX-1 and COX-2). The anti-inflammatory and analgesic properties of NSAIDs are mediated by inhibition of COX-2, whereas gastrointestinal toxicity arise from inhibition of COX-1. Therefore, use of agents that selectively inhibit COX-2 should decrease the risk of gastrointestinal complications. Several such drugs were developed in the 1990s and are collectively referred to as coxibs.

Although coxibs are associated with fewer gastrointestinal side effects when compared with traditional NSAIDs, the risk is still higher than with placebo. A large meta-analysis of 639 randomized studies assessed the variable risk of gastrointestinal complications among individual NSAIDs and found that the risk of gastrointestinal complications was the lowest with coxibs (relative risk [RR] 1.81, 95% confidence interval [CI] 1.17-2.81; $P = .0070$), followed by diclofenac (RR 1.89, 95% CI 1.16-3.09; $P = .0106$), followed by ibuprofen

(RR 3.97, 95% CI 2.22-7.10; $P < .0001$), and finally naproxen (RR 4.22, 95% CI 2.71-6.56; $P < .0001$). Since celecoxib is a coxib, it would be the best choice for this patient.

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Question 28

An 80-year-old woman with a past medical history significant for coronary artery disease, hypertension, and diabetes mellitus who takes aspirin daily presents to the emergency department for evaluation of 1 episode of hematemesis after experiencing abdominal pain, nausea/vomiting, and diarrhea. The episode of hematemesis occurred 12 hours before presentation. The symptoms of abdominal pain, nausea/vomiting, and diarrhea all started 24 hours before presentation, after eating out at a restaurant. They have since ceased. Her blood pressure upon arrival was 145/54 mmHg, and her heart rate is 78 bpm. Her blood urea nitrogen is 13 mg/dL (reference range, 8-20 mg/dL), and her hemoglobin is 12.3 g/dL (reference range [female], 12-16 g/dL). She has melena on rectal examination.

The gastrointestinal team calculates her Glasgow-Blatchford score, and it is 1. They recommend discharge but the emergency department refuses. Based on which risk factor, not accounted for within the Glasgow-Blatchford score, would they perhaps be making their judgement?

- A. Presence of melena
- B. Presentation of hematemesis instead of coffee ground emesis
- C. Age
- D. History of coronary artery disease

CORRECT ANSWER C

RATIONALE

The Glasgow-Blatchford score does not take advancing age into account, despite it being a clear risk factor for outcomes such as rebleeding and mortality. Although the guidelines suggest discharge of patients with a Glasgow-Blatchford score of 0-1 ($\leq 1\%$ chance of needing a hospital-based intervention or death), the recommendation is conditional and based on very low quality evidence. There are currently no randomized controlled trials proving safety of discharge in elderly patients with evidence of upper gastrointestinal bleeding. Furthermore, the guidelines acknowledge patient and provider preferences regarding certainty of risk and encourage the need to individualize decisions based on patient age, comorbidities, reliability, social support, and accessibility to medical care after discharge. Hence it would be reasonable in this case for the emergency department to admit the patient to the hospital.

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Question 29

A 36-year-old woman with a past medical history significant for chronic lower back pain presents to the emergency department with an episode of hematemesis. She has been taking ibuprofen 800 mg three times daily for the last 2 weeks. Her initial blood pressure is 89/56 mmHg, and her heart rate is 114 bpm. Her hemoglobin is 6.7 g/dL (reference range [female], 12-16 g/dL). She is given intravenous fluids and a histamine blocker. She undergoes an upper endoscopy within 12 hours of presentation and is found to have an 18- to 20-mm ulcer in the duodenal bulb with multiple flat red spots. No endoscopic therapy is given, and after the endoscopy, oral proton pump inhibitor (PPI) treatment is initiated. Two days later, she develops recurrent hematemesis with hypotension.

What risk factor identified above places her at a high risk of further bleeding?

- A. Hypotension on arrival to the emergency department
- B. Ulcer size
- C. PPI was not started before endoscopy
- D. Chronic and heavy use of nonsteroidal antiinflammatory drugs
- E. Lack of endoscopic therapy at index endoscopy

CORRECT ANSWER: B

RATIONALE

Ulcers larger than 1-2 cm are associated with increased rates of further bleeding with conservative therapy and after endoscopic therapy. Hemodynamic instability at the time of presentation is a risk factor for needing an urgent hospital-based intervention such as an upper endoscopy. Pre-endoscopic use of PPI does not lower the risk

of further bleeding and has only been shown to decrease the need for endoscopic intervention at the index endoscopy. Heavy nonsteroidal antiinflammatory drugs use is related to development of peptic ulcer disease but does not predict further bleeding. Endoscopic treatment for red flat spots is not recommended.

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Question 30

A 65-year-old man with a past medical history significant for peptic ulcer disease and coronary artery disease, who is receiving aspirin presents to the emergency department with melena. He reports feeling fatigued, with some dyspnea on exertion. His blood pressure is 143/67 mmHg, and his heart rate is 76 bpm. His hemoglobin is 7.1 g/dL (reference range [male], 14-18 g/dL), and his baseline hemoglobin level is close to 13 g/dL. His platelet count is 245,000/μL (reference range, 150,000-450,000/μL). His electrocardiogram

shows nonspecific T-wave inversions in all leads. What would be the next best step in the management of this patient?

- A. Admit to the medical intensive care unit
- B. Start an octreotide infusion
- C. Begin a platelet transfusion since he is receiving aspirin
- D. Give 1 unit of packed red blood cells with goal hemoglobin level of 8 g/dL

CORRECT ANSWER: D

RATIONALE

For the general population of patients with anemia, not restricted to upper gastrointestinal bleeding (UGIB), current US guidelines make a strong recommendation for a restrictive red blood cell transfusion threshold of 7 g/dL in hospitalized hemodynamically stable patients, including critical care patients, and a threshold of 8 g/dL in those undergoing orthopedic or cardiac surgery and those with existing cardiovascular disease. These recommendations were based on a systematic review indicating that restrictive transfusion policies reduced the number of patients receiving red blood cell transfusion by 43% with no evidence of an impact on clinically important outcomes. Given a paucity of randomized trial evidence in patients with UGIB with pre-existing cardiovascular disease, the current guidelines suggest using a threshold of 8 g/dL in such patients.

The patient is hemodynamically stable and does not meet criteria for intensive care unit admission in most institutions. There is insufficient evidence to suggest use of octreotide as pre-endoscopic medical therapy of nonvariceal UGIB. Platelet transfusion in the management of bleeding in this stable patient is not recommended, especially if they were at risk of demand ischemia.

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Question 31

A 74-year-old man with a past medical history significant for coronary artery disease, who is receiving aspirin 81 mg daily presents to the emergency department with repeated episodes of painless hematochezia. His blood pressure is 78/45 mmHg, and his heart rate is 97 bpm. He appears pale but otherwise offers no complaints. His electrocardiogram is normal. He is admitted to the medical intensive care unit, and a bedside upper endoscopy is being planned. After fluid resuscitation, his blood pressure and heart rate normalize.

Laboratory results are below.

Laboratory Test	Result	Reference Range
Creatinine, serum, mg/dL	1.1	0.7-1.5
Hemoglobin, blood, g/dL	8.7	Male: 14-18
Platelet count, plt/ μ L	150,000	150,000-450,000

The primary team would like to transfuse him with 1 pool of platelets to mitigate the effects of aspirin.

What should you advise them?

- A. Give 1 pool of platelets
- B. Give 1 dose of desmopressin
- C. Give 1 unit of fresh frozen plasma
- D. Proceed with urgent upper endoscopy

CORRECT ANSWER: D

RATIONALE

Although the American Society for Gastrointestinal Endoscopy (ASGE) guidelines propose that platelet transfusion is an option for patients who take antiplatelet agents and have serious gastrointestinal bleeding, no evidence is presented to support this practice. A recent retrospective study showed that platelet transfusions in patients with gastrointestinal bleeding who are taking antiplatelet agents without thrombocytopenia did not reduce rebleeding but was associated with higher mortality.

There is no indication for use of either desmopressin or fresh frozen plasma in this otherwise healthy patient.

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Question 32

A 34-year-old woman with a past medical history significant for metastatic melanoma presents to the emergency department with repeated episodes

of painless hematochezia. Her blood pressure is 89/34 mmHg, and her heart rate is 123 bpm. Her hemoglobin is 6.3 g/dL (reference range [female], 12-16 g/dL), and her platelets are 323,000/ μ L (reference range, 150,000-450,000/ μ L). She is not receiving any antithrombotic agents. She is given 2 L of saline and 1 unit of packed red blood cells after which her hypotension resolves. A nasogastric (NG) tube is placed, and the gastrointestinal team has been asked to evaluate the patient.

Which of the following is true?

- A. Placement of an NG tube will help in clearing clots from the stomach
- B. A bilious aspirate suggests that the source of bleeding is NOT in the upper gastrointestinal tract
- C. A clear aspirate suggests that the source of bleeding is NOT in the upper gastrointestinal tract
- D. An NG lavage is not required to diagnose, provide prognostic information, or improve visualization during upper endoscopy in patients with upper gastrointestinal bleeding
- E. Lavage with iced saline will help stop bleeding from the upper gastrointestinal tract

CORRECT ANSWER: D

RATIONALE

A clear or bile-stained NG aspirate may be seen in up to 18% of patients with an upper gastrointestinal source of bleeding. In a Canadian upper gastrointestinal bleeding registry, 15% of patients with a clear/bile-stained aspirate had an active bleeding or nonbleeding visible vessel compared with 23% with coffee-grounds and 43% with bloody aspirates. Furthermore, physicians are incorrect about 50% of the time in accurately identifying nonbloody bile-stained aspirate. It is also unclear whether a bloody aspirate provides better prognostic information than other readily available data such as blood pressure and heart rate. A standard, small-bore NG tube typically used for aspiration is not likely to effectively clear

clots from the stomach. A large bore orogastric tube is more likely to be successful. Lastly, older textbooks have suggested use of iced saline to lavage the stomach to stop bleeding. However, studies in dogs with experimentally induced ulcers indicated that results with lavage are no better and may even be worse at temperatures of 0 °C to 4 °C

Based on this data, current guidelines do not recommend the placement of an NG tube for diagnosis, prognosis, visualization, or therapeutic effect in patients with UGIB.

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Question 33

A 43-year-old man with a past medical history significant for obesity and hypertension presented to the emergency department with hematemesis. His blood pressure was 64/36 mmHg, and his heart rate was 134 bpm. He was given 2 L of saline after which his blood pressure and heart rate normalized. His hemoglobin was 9.3 g/dL (reference range [male], 14-18 g/dL).

He was given proton pump inhibitor bolus plus continuous infusion, and an upper endoscopy was being planned. Before his upper endoscopy, he was given an infusion of erythromycin 250 mg over 30 minutes.

What does the addition of erythromycin to the pre-endoscopic management of this patient potentially decrease?

- A. Need for blood transfusions
- B. Length of hospitalization
- C. Risk of further bleeding
- D. Risk of mortality

CORRECT ANSWER: B

RATIONALE

Evidence from randomized studies is lacking for benefit of erythromycin in reducing further bleeding, transfusion need, and mortality. Studies, however, show meaningful reductions in need for repeat endoscopies and length of hospitalizations in addition to increasing visualization during endoscopy.

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Question 34

A 39-year-old man with a past medical history significant for nonsteroidal antiinflammatory drug-related peptic ulcer disease presents to the emergency department with an episode of hematemesis. He is hemodynamically stable and has not had recurrent episodes of hematemesis. His physical examination is unremarkable. His hemoglobin is 8.9 g/dL (reference range [male], 14-18 g/dL). He is given intravenous fluids and intravenous proton pump inhibitor.

What would be the next best step in the management of this patient?

- A. Give erythromycin infusion, 250 mg, over 30 minutes
- B. Prophylactically intubate the patient to avoid aspiration
- C. Perform an nasogastric (NG) lavage with iced saline
- D. Transfuse 1 unit of packed red blood cells

CORRECT ANSWER: A

RATIONALE

The rationale behind use of a prokinetic agent like erythromycin is to move blood and clots more distally to improve visualization and diagnosis during endoscopy. Although randomized controlled trials lack evidence to show a decrease in rebleeding, they have shown a reduction in the need for repeat endoscopies and length of hospitalization.

Prophylactic endotracheal intubation for airway protection during an upper endoscopy for upper gastrointestinal bleeding has not consistently shown to decrease cardiopulmonary complications. It is likely beneficial in a small subset of patients at risk of aspiration, such as cases of massive upper gastrointestinal bleeding or in a patient with altered mental status.

Older textbooks have suggested use of iced saline to lavage the stomach to stop bleeding. However, most bleeding halts spontaneously; hence, the benefit is not clear. Furthermore, studies in dogs with experimentally induced ulcers indicated that results with lavage are no better and may even be worse at temperatures of 0 °C to 4 °C

Current US guidelines recommend a restrictive policy of red blood cell transfusion with a threshold for transfusion at a hemoglobin of 7 g/dL in otherwise healthy patients who present with upper gastrointestinal bleeding. There is no indication for transfusion in this patient.

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Question 35

A 46-year-old woman with a past medical history significant for hypertension and hyperlipidemia presents to the emergency department after several episodes of hematemesis. She endorses having a similar episode 1 year ago, during which time she underwent an upper endoscopy and was diagnosed with a gastric ulcer. Her blood pressure on arrival is 103/45 mmHg, and her heart rate is 107 bpm. Her hemoglobin is 9.6 g/dL (reference range [female], 12-16 g/dL). She is given intravenous fluids. There is a severe shortage of intrave-

nous proton pump inhibitors in the hospital, and she cannot be given this medication.

What would be the next best step in the management of this patient?

- A. Start histamine blocker intravenous infusion
- B. Start octreotide infusion
- C. Give oral misoprostol
- D. Proceed to endoscopy

CORRECT ANSWER: D

RATIONALE

Available evidence suggests no benefit in clinical outcomes such as rebleeding in patients who receive pre-endoscopic proton pump inhibitor therapy. Clinical trials do not support the use of either histamine blockers or misoprostol in the management of nonvariceal upper gastrointestinal bleeding. Although octreotide can be theoretically beneficial, there is no clear scientific evidence supporting its routine use.

Therefore, proceeding to endoscopy in a timely fashion (within 24 hours) is the next best step in the management of this patient.

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Question 36

A 54-year-old woman with a past medical history significant for coronary artery disease, who is receiving aspirin 81 mg daily presents to the emergency department for evaluation of melena. She is found to have a clean-based duodenal ulcer. On biopsies, she is found to have *Helicobacter pylori* (*H pylori*) infection. She is given antibiotics and eradication of *H pylori* is subsequently documented several weeks later. To decrease her risk of developing ulcers in the future, what should be done next?

- A. Stop aspirin as she does not need this anymore
- B. Halt use of proton pump inhibitor (PPI) since *H pylori* has been successfully eradicated
- C. Start sucralfate treatment as it will protect the lining of the stomach
- D. Continue PPI so long as patient is to continue receiving aspirin

CORRECT ANSWER: D

RATIONALE

The benefit of taking low-dose aspirin in patients with established cardiovascular disease for secondary prophylaxis is clear and delayed resumption after ulcer bleeding is associated with an increased risk in mortality.

In a trial performed in *H pylori*-positive patients with ulcer complications receiving low-dose aspirin, significantly less recurrent ulcer bleeding at 12 months was seen in patients taking PPI therapy versus placebo (1.6% vs 14.8%). Hence, patients with bleeding ulcers who require continued antiplatelet therapy should be prescribed once-daily PPI.

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Question 37

A 63-year-old man with a past medical history significant for stroke, currently receiving aspirin 81 mg daily, presents to the emergency department with melena. His aspirin is stopped, and he is sent for an urgent upper endoscopy. He is found to have a gastric ulcer with a visible vessel. This is treated with bipolar cautery and subsequently he starts proton pump inhibitors. On hospital day 1, he is doing well and resumes a liquid diet.

The primary team is inquiring when he can resume use of aspirin.

What would you advise the team?

- A. Stop aspirin indefinitely since resumption will place him at high risk of rebleeding
- B. Resume aspirin at day 3, provided he shows no signs of rebleeding
- C. Resume aspirin in 14 days to protect him from rebleeding
- D. Resume aspirin in 30 days to protect him from rebleeding

CORRECT ANSWER: B

RATIONALE

The benefit of taking low-dose aspirin in patients with established cardiovascular disease for secondary prophylaxis is clear and delayed resumption after ulcer bleeding is associated with an increased risk in mortality.

Joint consensus recommendations from US cardiology and GI organizations stated that “reintroduction of antiplatelet therapy in high-cardiovascular-risk patients is reasonable in those who remain free of rebleeding after 3–7 days.” A study from Hong Kong indicated a benefit of resumption of low-dose aspirin immediately after endoscopic hemostasis in patients with high-risk stigmata. Thus, current US guidelines suggest that early resumption of antiplatelet therapy within 1 to 3 days after hemostasis, and certainly within 7 days, will be appropriate in most patients with established cardiovascular disease.

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Question 38

A 42-year-old man with a past medical history significant for diet-controlled diabetes mellitus presents to the emergency department for evaluation of melena. He does not take any medications. He is found to have a 6- to 8-mm duodenal ulcer with a nonbleeding visible vessel. This is treated with bipolar cautery. Random gastric biopsies are

not suggestive of *Helicobacter pylori* (*H pylori*) infection. He is discharged home on twice-daily oral proton pump inhibitor (PPI). To decrease his risk of developing recurrent ulcers, what should be done at his next clinic visit, which is scheduled 2 weeks from his index endoscopy?

- A. Empirically treat him for *H pylori*
- B. Continue twice-daily oral PPI and continue indefinitely
- C. Decrease his oral PPI to once daily and continue indefinitely
- D. Stop his PPI after 6-8 weeks of treatment
- E. Start aspirin 81 mg daily for primary prophylaxis

CORRECT ANSWER: C

RATIONALE

Patients with idiopathic bleeding ulcers (not non-steroidal antiinflammatory drugs or *H pylori*) have a high rate of recurrence if they are not treated with protective co-therapy. Although no randomized trials have assessed the role of medical co-therapy, it is reasonable to assume that antiulcer therapy will reduce the risk of recurrent ulceration.

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Question 39

A 52-year-old woman with severe osteoarthritis of the knee requiring heavy and regular use of meloxicam presents to the clinic. She has a history of gastric ulcers with at least 1 documented hospitalization for gastrointestinal bleeding. She is tested for *Helicobacter pylori* via stool antigen and is negative. Despite multiple attempts, she is unable to wean herself off meloxicam. What should you recommend?

- A. Continue meloxicam and start once-daily oral proton pump inhibitor (PPI)
- B. Continue meloxicam and start twice-daily oral PPI
- C. Switch to celecoxib and start once-daily oral PPI
- D. Switch to celecoxib with no need to add daily PPI

CORRECT ANSWER: C

RATIONALE

Several randomized trials have studied this issue and have shown that patients with bleeding ulcers while receiving nonsteroidal antiinflammatory drugs (NSAIDs) who must continue NSAID treatment should receive a cyclooxygenase-2 (COX-2)-selective NSAID at the lowest effective dose plus PPI therapy.

Meloxicam is not a selective COX-2-selective NSAID, hence the patient should be switched to celecoxib and started with once-daily PPI.

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Question 40

A 39-year-old woman presents to the emergency department with melena. She undergoes an urgent upper endoscopy that shows an ulcer in the antrum with an adherent clot. What would be the appropriate management in this case?

- A. Epinephrine injection applied to the ulcer base
- B. No endoscopic intervention; patient can be started on high-dose proton pump inhibitor (PPI)
- C. No endoscopic intervention; patient can be started on low-dose PPI
- D. No endoscopic intervention; patient can be discharged home

CORRECT ANSWER: B

RATIONALE

The most recent meta-analysis of randomized controlled trials did not find benefit in further bleeding or mortality when endoscopic therapy was compared with no endoscopic therapy in patients with adherent clots.

Current US guidelines suggest the use of high-dose PPI for treatment of high-risk patients with upper gastrointestinal bleeding due to ulcers who received endoscopic hemostatic therapy until 2 weeks after the index endoscopy. They define this as twice-daily oral PPI. Thereafter, the patient can be switched to once-daily dosing for another 2 weeks. This recommendation is based on a randomized controlled trial that showed a decrease in bleeding at 14 and 28 days after the index endoscopy with use of high-dose PPI.

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Question 41

An 82-year-old man is admitted to the hospital with urosepsis. During the hospitalization, he develops melena and becomes hemodynamically unstable. An urgent upper endoscopy shows an oozing ulcer along the lesser curvature of the stomach. It is treated with epinephrine and bipolar cautery. Two days later, he becomes hemodynamically unstable again and is found to have persistent melena. He undergoes a repeat upper endoscopy that shows a nonbleeding visible vessel within the base of the same ulcer seen during his index endoscopy. What would be the treatment of choice in this scenario?

- A. Retreatment with epinephrine and bipolar cautery
- B. Standard through-the-scope clips
- C. Over-the-scope clip
- D. Transcatheter arterial embolization instead of endoscopic therapy

CORRECT ANSWER: C

RATIONALE

Current U.S. guidelines recommend repeating an

upper endoscopy and endoscopic therapy, rather than surgery or transcatheter arterial embolization (TAE), in patients with bleeding ulcers that were initially treated with endoscopic therapy. Studies show that a second application of endoscopic therapy was successful in prevention of further bleeding in most patients and was associated with fewer complications than surgery. Although no randomized controlled trials have compared repeat endoscopy to TAE, given the high success rate of repeat endoscopic therapy as well as safety, it is recommended over TAE.

Furthermore, a randomized controlled trial revealed that over-the-scope clips were superior to standard therapy in further bleeding (15.2% vs 57.6%). Standard through-the-scope clips were the therapy used in 94% of the control group, potentially limiting generalizability of this study regarding comparisons of over-the-scope clips to other forms of hemostatic therapy.

Repeated applications of thermal contact therapy should probably be avoided based on evidence that showed that approximately half of the perforations reported with heater probes occurred in patients receiving 2 consecutive treatments during the same hospitalization. Alternative forms of hemostatic therapy should be considered if thermal contact was used at the initial endoscopy.

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Schmidt A, Golder S, Goetz M, et al. Over-the-Scope Clips Are More Effective Than Standard Endoscopic Therapy for Patients With Recurrent Bleeding of Peptic Ulcers. *Gastroenterology*. 2018;155(3):674-686.e6. doi:10.1053/j.gastro.2018.05.037

Question 42

A 62-year-old woman with a past medical history significant for hypertension presents to clinic with complaints of 1 episode of hematemesis 1 week before presentation. She is hemodynamically stable and complains of nonspecific abdominal discomfort. She only takes hydrochlorothiazide 25 mg once daily. A *Helicobacter pylori* (*H pylori*) stool antigen is negative. An upper endoscopy finds a large 15-mm clean gastric ulcer in the body of the stomach. It appears to be deep and chronic in appearance with heaped-up borders. A biopsy of the edge of the ulcer shows significant oozing, so no further biopsies are done. Pathology shows no evidence of malignancy.

In addition to starting an oral proton pump inhibitor (PPI), what should you do next?

- A. Continue PPI indefinitely
- B. Repeat upper endoscopy in 8-12 weeks to document healing
- C. Evaluate patient with endoscopic ultrasound
- D. Empirically treat patient for *H pylori* infection

CORRECT ANSWER: B

RATIONALE

In patients with gastric ulcers, follow-up endoscopy in 8 to 12 weeks is suggested to demonstrate healing. The basis of this recommendation is that a small proportion of gastric ulcers are secondary to a gastric neoplasm. PPI therapy may be able to

heal these ulcers and hence mask these cancers. Hence, biopsies at the index and follow-up endoscopy are recommended.

Although this recommendation has been challenged in the era of increased nonsteroidal anti-inflammatory drug use and related gastric ulcers, in this patient a repeat endoscopy is appropriate given the appearance of the ulcer, insufficient biopsies at the index endoscopy (due to bleeding), advancing age, and lack of clear cause for the gastric ulcer (*H pylori*-negative and no nonsteroidal antiinflammatory drug use).

REFERENCE

Farinati F, Cardin F, Di Mario F, et al. Early and advanced gastric cancer during follow-up of apparently benign gastric ulcer: significance of the presence of epithelial dysplasia. *J Surg Oncol*. 1987;36(4):263-267. doi:10.1002/jso.2930360410

Question 43

A 64-year-old man presents to the emergency department with melena. He undergoes an upper endoscopy that shows an oozing gastric ulcer. This is treated with both epinephrine injection and bipolar cautery. After endoscopy, he receives 80 mg of intravenous pantoprazole followed by a continuous infusion of 8 mg/hr for 72 hours. He is discharged with oral pantoprazole 40 mg twice daily and a follow-up appointment in clinic is made for the week after discharge.

What is the rationale for the use of high-dose proton pump inhibitor (PPI) after endoscopic treatment for ulcer bleeding?

- A. Promote clot formation and stability
- B. Prevent the formation of new ulcers
- C. Mitigate the effects of *Helicobacter pylori* infection
- D. Avoid pain that maybe induced by ulcer formation

CORRECT ANSWER: A

RATIONALE

In vitro data has shown that reduction in intragastric acid promotes clot formation and stability. This is the basis by which PPI therapy is used after successful endoscopic treatment of bleeding ulcers. It remains unclear whether the target intragastric pH should be near 7 or whether inhibition of pepsin-induced clot lysis at a pH of 4 to 5 is adequate. PPI therapy will help with eventual healing and prevention of recurrent ulcers but that is not the rationale behind its immediate use after achieving successful endoscopy hemostatic therapy in patients with bleeding ulcers.

REFERENCES

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Green FW Jr, Kaplan MM, Curtis LE, Levine PH. Effect of acid and pepsin on blood coagulation and platelet aggregation. A possible contributor prolonged gastroduodenal mucosal hemorrhage. *Gastroenterology*. 1978;74(1):38-43.

Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG Clinical Guideline: Upper Gastrointestinal and Ulcer Bleeding. *Am J Gastroenterol*. 2021;116(5):899-917. doi:10.14309/ajg.0000000000001245

Patchett SE, Enright H, Afdhal N, O'Connell W, O'Donoghue DP. Clot lysis by gastric juice: an in vitro study. *Gut*. 1989;30(12):1704-1707. doi:10.1136/gut.30.12.1704

Question 44

A 42-year-old woman presents to the emergency department with 1 episode of hematemesis. She undergoes an urgent upper endoscopy that shows a 6- to 8-mm duodenal ulcer with a nonbleeding visible vessel that is treated with standard through-the-scope clips.

What is the appropriate next step in her management?

- A. Start pantoprazole continuous infusion of 8 mg/hr for 72 hours
- B. Start pantoprazole 80 mg intravenous (IV) bolus x 1 followed by pantoprazole 40 mg IV three times daily for 72 hours
- C. Start oral pantoprazole 40 mg twice daily for 72 hours
- D. Start pantoprazole 40 mg IV daily for 72 hours

CORRECT ANSWER: B

RATIONALE

The current US guidelines make a strong recommendation for the use of high-dose proton pump inhibitor therapy given continuously or intermittently for 3 days after successful endoscopic hemostatic treatment. This is based on high-quality evidence that documents a large reduction in further bleeding and mortality when compared with placebo. Furthermore, high-dose proton pump inhibitor therapy is defined as 80 mg or more daily for 3 or more days. Continuous therapy should be 80 mg bolus followed by 8 mg/hr infusion. By contrast, the optimal dosing with intermittent oral or intravenous therapy is uncertain, although the guidelines suggest an 80 mg bolus followed by 40 mg 2 to 4 times daily. Intermittent doses can be given orally assuming the patient is awake, alert, and without nausea/vomiting or dysphagia.

REFERENCE

Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG Clinical Guideline: Upper Gastrointestinal and Ulcer Bleeding. *Am J Gastroenterol*. 2021;116(5):899-917. doi:10.14309/ajg.0000000000001245

Question 45

A 72-year-old man with a past medical history significant for insulin-dependent diabetes mellitus coronary artery disease receiving aspirin, and end-stage renal disease receiving hemodialysis pres-

ents to the emergency department with painless hematochezia. His blood pressure is 75/43 mmHg, and his heart rate is 119 bpm. He receives intravenous fluids after which his blood pressure rises to 97/54 mmHg, and his heart rate is 108 bpm. He has another episode of hematochezia in the emergency department. He is sent for urgent computed tomography angiogram, but no extravasation of contrast is noted. Review of records show that he underwent an upper endoscopy and colonoscopy 1 month ago for Barrett esophagus and colorectal cancer screening. Both were good quality examinations and only showed 1 small tubular adenoma in the sigmoid colon.

Later that night, the patient has 2 more episodes of hematochezia with hemodynamic instability. He is transferred to the intensive care unit and appropriately resuscitated using intravenous fluids and packed red blood cells.

What would be the next best step in identifying the source of bleeding?

- A. Tagged red blood cell scintigraphy
- B. Repeat computed tomography angiogram
- C. Push enteroscopy
- D. Rapid bowel preparation followed by colonoscopy

CORRECT ANSWER: C

RATIONALE

Since this patient recently underwent endoscopic examinations of the upper and lower gastrointestinal tract, which failed to reveal a source of bleeding, it would be reasonable to assume that the etiology of bleeding is in the small bowel. A push enteroscopy can allow for evaluation of the upper gastrointestinal tract to the proximal jejunum. Most bleeding lesions are found in the proximal small bowel, making this a desirable examination to pursue next.

REFERENCE

Kovacs TO, Jensen DM. Recent advances in the

endoscopic diagnosis and therapy of upper gastrointestinal, small intestinal, and colonic bleeding. *Med Clin North Am.* 2002;86(6):1319-1356. doi:10.1016/S0025-7125(02)00079-2

Question 46

An 82-year-old man with a past medical history significant for coronary artery disease, lower extremity deep venous thrombosis being treated with warfarin, and lower back pain presents to your clinic after recently being discharged from the hospital for his first episode of diverticular bleeding. During colonoscopy, he was found to have diverticulosis of the sigmoid colon. Before discharge, it is determined that he no longer needs to receive warfarin since he completed his therapy for a provoked deep venous thrombosis. Review of his discharge medications show that he is taking naproxen near daily along with aspirin 81 mg daily. To lower his risk of recurrent diverticular bleeding, what should you recommend?

- A. Surgical evaluation for sigmoidectomy
- B. Stop aspirin 81 mg daily
- C. Stop use of naproxen
- D. Initiate a high-fiber diet

CORRECT ANSWER: C

RATIONALE

Several studies have indicated that nonsteroidal antiinflammatory drugs (NSAIDs) increase the risk of both incident and recurrent lower gastrointestinal bleeding. A prospective study of 132 patients hospitalized with diverticular bleeding found that recurrence was 77% among patients who continued NSAIDs versus 9% in those who discontinued. Based on this and other data, the current US guidelines recommend avoidance of nonaspirin NSAIDs in patients with a history of acute lower gastrointestinal bleeding particularly if secondary to diverticulosis or angioectasias. They also recommend continuation of aspirin in patients with established cardiovascular disease for the purpose of secondary prevention.

Although surgical evaluation and sigmoidectomy is an option in this patient, they would be at high risk of procedural complications. Also, given that they have only had 1 episode of diverticular bleeding, conservative management would be preferred. A high-fiber diet is not associated with a decreased risk of recurrent diverticular bleeding.

REFERENCES

Nagata N, Niikura R, Aoki T, et al. Impact of discontinuing non-steroidal antiinflammatory drugs on long-term recurrence in colonic diverticular bleeding. *World J Gastroenterol.* 2015;21(4):1292-1298. doi:10.3748/wjg.v21.i4.1292

Strate LL, Gralnek IM. ACG Clinical Guideline: Management of Patients With Acute Lower Gastrointestinal Bleeding [published correction appears in *Am J Gastroenterol.* 2016 May;111(5):755]. *Am J Gastroenterol.* 2016;111(4):459-474. doi:10.1038/ajg.2016.41

Question 47

A 57-year-old woman with a past medical history significant for congestive heart failure, stroke, and atrial fibrillation presents for her first screening colonoscopy. She takes dabigatran daily but held it for 1 day before her examination. During her procedure, she is found to have a 9- to 10-mm sessile polyp in the right colon.

What would be the best approach to minimize her risk of delayed bleeding after polypectomy?

- A. Hold dabigatran for the next 7 days
- B. Hold the dabigatran for another night, keep the patient on clear liquids, and repeat the procedure with polypectomy the following day
- C. Use snare electrocautery polypectomy technique
- D. Use cold snare polypectomy technique

CORRECT ANSWER: D

RATIONALE

For polyps smaller than 10 mm, cold snare polypectomy is associated with a lower risk of delayed bleeding after polypectomy in anticoagulated patients. Polyps smaller than 10 mm can be completely resected using cold snare. The polyps also have smaller blood vessels that often do not require electrocautery for safe resection. Furthermore, use of snare electrocautery can expand the zone of necrosis at the polypectomy site and cause delayed bleeding after polypectomy.

Holding anticoagulation for a protracted time in a patient at high risk of stroke from atrial fibrillation carries risk, and this is likely not outweighed by the benefit of avoiding bleeding after polypectomy.

REFERENCES

Horiuchi A, Nakayama Y, Kajiyama M, Tanaka N, Sano K, Graham DY. Removal of small colorectal polyps in anticoagulated patients: a prospective randomized comparison of cold snare and conventional polypectomy. *Gastrointest Endosc*. 2014;79(3):417-423. doi:10.1016/j.gie.2013.08.040

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Takeuchi Y, Mabe K, Shimodate Y, et al. Continuous Anticoagulation and Cold Snare Polypectomy Versus Heparin Bridging and Hot Snare Polypectomy in Patients on Anticoagulants With Subcentimeter Polyps: A Randomized Controlled Trial. *Ann Intern Med*. 2019;171(4):229-237. doi:10.7326/M19-0026

Question 48

A 67-year-old woman with no significant past medical history presents to the emergency department with acute onset of left-sided abdominal pain and cramping followed by 2 episodes

of hematochezia. Her blood pressure on arrival is 105/65 mmHg, and her heart rate is 79 bpm. Her pain is improved from a few hours ago. Her abdominal examination is significant for mild discomfort in the left lower quadrant without rebound or guarding. She is a marathon-runner and as of late has been suffering from pain in her knees. This morning before her run, she took 800 mg of ibuprofen. Her last colonoscopy was a good quality examination done 2 years ago and was normal. She has no family history of colorectal cancer.

What is the most likely underlying cause for hematochezia?

- A. Diverticular bleeding
- B. Ischemic colitis
- C. Mesenteric ischemia
- D. Malignancy

CORRECT ANSWER: B

RATIONALE

Acute onset of abdominal pain/cramping followed by hematochezia is most consistent with a diagnosis of ischemic colitis. In this case, the patient is otherwise stable and clinically improving. Her risk factors for ischemia includes her age, use of nonsteroidal antiinflammatory drugs, and possible dehydration related to her marathon run. Early colonoscopy with biopsies can establish this diagnosis.

Her presentation is inconsistent with mesenteric ischemia, and she has no risk factors. Pain is not a feature of diverticular bleeding. She is at average risk of developing colorectal cancer and given the results of her recent colonoscopy, malignancy is much less likely.

REFERENCE

Brandt LJ, Feuerstadt P, Longstreth GF, Boley SJ; American College of Gastroenterology. ACG clinical guideline: epidemiology, risk factors, patterns of presentation, diagnosis, and management of colon ischemia (CI). *Am J Gastroenterol*. 2015;110(1):18-45. doi:10.1038/ajg.2014.395

Question 49

A 39-year-old healthy woman presents to clinic with complaints of hematochezia. She reports noting fresh blood in the toilet and when she wipes. This has been ongoing for several months now. She endorses passage of hard stools. She denies weight loss and abdominal/rectal pain. She is hemodynamically stable. On rectal examination, no abnormalities are noted.

What is the best next step in the management of this patient?

- A. Prescribe a fiber supplement and Sitz baths
- B. Admit to the hospital
- C. Perform an outpatient colonoscopy
- D. Check her hemoglobin and only pursue a workup if she is anemic

CORRECT ANSWER: C

RATIONALE

The bleeding is chronic, and the source is likely anorectal based on the description of symptoms. Passage of hard stools makes hemorrhoids the most likely etiology. Internal hemorrhoids cannot be evaluated on a simple rectal examination. However, given the rise in incidence of colorectal cancer (particularly rectal cancer) in younger patients, it would be appropriate to pursue a colonoscopy and rule out this possibility first.

The patient is stable and does not need hospitalization. A workup should be pursued irrespective of whether the patient develops anemia since rectal bleeding is considered a red-flag symptom.

REFERENCE

Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal Cancer Incidence Patterns in the United States, 1974-2013. *J Natl Cancer Inst.* 2017;109(8):djw322. doi:10.1093/jnci/djw322

Question 50

A 61-year-old woman with a past medical history

significant for hypertension presents to the emergency department with hematemesis. She has no prior history of peptic ulcer disease and denies use of nonsteroidal antiinflammatory drugs. She does not take any medications. She is hemodynamically stable and undergoes an upper endoscopy, which shows a large, cratered ulcer in the gastric antrum. Biopsies of the ulcer are taken. They show the presence of uniform spindle cells with elongated nuclei and eosinophilic cytoplasm, growing in fascicles. There is minimal pleomorphism and a mitotic rate of 5 to 10 per 50 high-power fields. Further testing shows presence of a *KIT* mutation.

What is the diagnosis?

- A. Nonsteroidal antiinflammatory drug-associated peptic ulcer disease
- B. Gastric adenocarcinoma
- C. Gastrointestinal stromal tumor
- D. Gastric carcinoid

CORRECT ANSWER: C

RATIONALE

The presence of well-organized spindle cells and a *KIT* mutation is suggestive of a gastrointestinal stromal tumor. Spindle cells are not seen in benign ulcers or gastric adenocarcinomas and lymphomas.

REFERENCE

Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumors: a consensus approach. *Int J Surg Pathol.* 2002;10(2):81-89. doi:10.1177/106689690201000201

CHAPTER 13

Inflammatory bowel disease

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Question 1

You meet a 52-year-old woman referred to you for evaluation of bloody diarrhea. She tells you that she started having loose bowel movements multiple times a day about 6 weeks ago, but 2 weeks ago she started noticing blood in her bowel movements and she is very worried. Upon further questioning, you elicit that she has mild abdominal pain, has lost 5 pounds in the past 4 weeks, and has been noticing that her knees and ankles are hurting more. You order blood work, and it is all unremarkable.

What is the next best step in her management?

- A. Order computed tomography
- B. Tell her to take probiotics and the diarrhea will improve
- C. Prescribe hyoscyamine for the treatment of irritable bowel syndrome
- D. Order a colonoscopy
- E. Order a stool test to evaluate for *Clostridium difficile*

CORRECT ANSWER: E

RATIONALE

Her presentation raises concern for ulcerative colitis, and she certainly merits a colonoscopy. Depending on the severity of her abdominal pain, cross-sectional imaging could be considered as well. However, the next step while she is still in your office would be to obtain a stool sample to rule out *Clostridium difficile* infection as an etiology. It would not be appropriate

to send someone who is having bloody bowel movements, weight loss, and joint pain home on probiotics or antispasmodics without evaluating for other etiologies first.

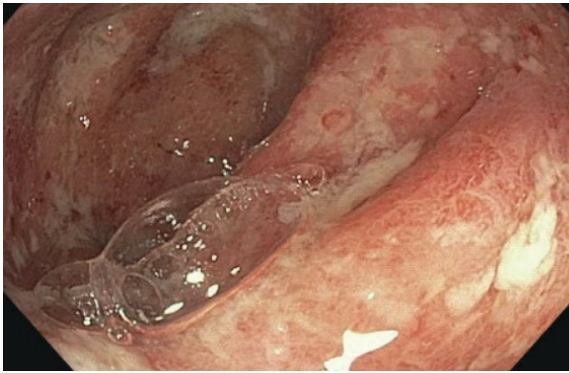
REFERENCE

Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol*. 2019;114(3):384-413. doi:10.14309/ajg.0000000000000152

Question 2

A 25-year-old woman presents in consultation for 3 months of diarrhea and rectal bleeding. She has no medical problems and was in her usual state of health until 3 months earlier when she was on a cruise and developed a gastroenteritis along with other members of her family. Her family all recovered in 3 days, but she had persistent diarrhea with up to 4 loose bowel movements daily. In a month, she started noticing blood in some of her stools. Last month, all of her stools had blood in them, and she was having as many as 10 bowel movements a day, including waking up at night. Her examination is notable for abdominal tenderness to gentle palpation. You order blood work, which is most notable for anemia with a hemoglobin of 10 g/dL (reference range [female]: 12-16 g/dL) and a serum albumin of 3.2 g/dL (reference range, 3.5-5.5 g/dL).

You perform a colonoscopy in your office that week and see the following:



In addition to a prednisone taper, what is the best medication to recommend?

- A. Mesalamine
- B. Budesonide
- C. Tofacitinib
- D. Infliximab
- E. Azathioprine

CORRECT ANSWER: D

RATIONALE

In adult patients with moderate to severe ulcerative colitis (UC), the American Gastroenterological Association (AGA) recommends using a biologic. In adult patients with moderate to severe UC, the AGA recommends against using thiopurine monotherapy for induction of remission. Tofacitinib can be used for the treatment of severe UC; however, tofacitinib is approved for patients who fail anti-tumor necrosis factor therapy.

REFERENCE

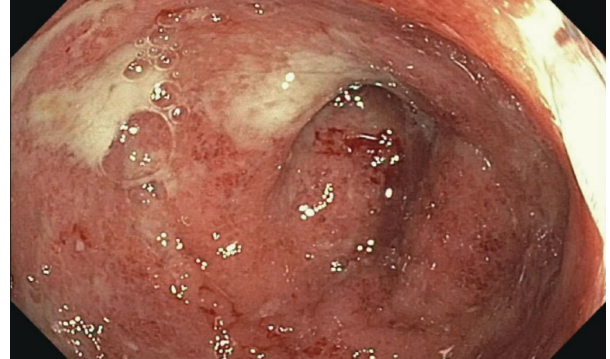
Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology*. 2020;158(5):1450-1461. doi:10.1053/j.gastro.2020.01.006

Question 3

A 30-year-old man with no known medical problems presents to your office for evaluation of 6 months of 3 loose bowel movements daily. One month ago, he started noticing blood in his stools and abdominal pain. He stopped eating food dur-

ing the day to control the number of bowel movements and amount of blood he is passing. He feels that explains why he lost 30 pounds over the past month. You order blood work, which is all normal.

You do a colonoscopy in your office the week after and see the following:



You prescribe a prednisone taper. The pathology report confirms a diagnosis of ulcerative colitis (UC).

Which of the following medications would be the most appropriate next step in treatment?

- A. Adalimumab
- B. Azathioprine
- C. Vedolizumab
- D. Methotrexate
- E. Tofacitinib

CORRECT ANSWER: C

RATIONALE

The VARSITY trial is the first head-to-head trial of biologic agents for the treatment of UC. The authors demonstrate that vedolizumab is superior to adalimumab for the induction and maintenance of patients with moderate to severe UC. Immunosuppressants should not be used as monotherapy for induction and maintenance of remission in severe UC. Tofacitinib is indicated for severe UC after failure of treatment with anti-tumor necrosis factor agents.

REFERENCES

Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA

Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology*. 2020;158(5):1450-1461. doi:10.1053/j.gastro.2020.01.006

Sands BE, Peyrin-Biroulet L, Loftus EV Jr, et al. Vedolizumab versus Adalimumab for Moderate-to-Severe Ulcerative Colitis. *N Engl J Med*. 2019;381(13):1215-1226. doi:10.1056/NEJMoa1905725

Question 4

You are seeing a 27-year-old woman with a recent diagnosis of severe pan ulcerative colitis. You prescribed infliximab, and she is back in the office 2 weeks after completing induction to follow-up as scheduled. She feels absolutely no difference after receiving 3 doses of infliximab 10 mg/kg and continues to have up to 8 bloody bowel movements daily including up to 1 nocturnal bowel movement.

What is the next best step in treatment?

- A. Start a prednisone taper until her next dose of infliximab
- B. Switch to adalimumab
- C. Switch to vedolizumab
- D. Increase the dose of infliximab
- E. Wait until the next dose of infliximab and if she still has no response, check a drug level

CORRECT ANSWER: C

RATIONALE

Primary nonresponse with anti-tumor necrosis factor agents is clinically diagnosed as having no change in symptoms after completion of induction. Given the severity of her symptoms, switching to a biologic with a different mechanism of action is indicated. She may certainly require a prednisone taper, but it should not be a bridge to the same biologic agent. Although therapeutic drug monitoring is beneficial for dose optimization, it is not needed for diagnosis of primary nonresponse.

REFERENCE

Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol*. 2019;114(3):384-413. doi:10.14309/ajg.0000000000000152

Question 5

You are seeing a 32-year-old male administrative assistant in clinic for follow-up after his colonoscopy, which was ordered for abdominal pain and rectal bleeding. You educate him about his diagnosis of Crohn's disease and recommend adalimumab therapy.

In addition to a complete blood count, metabolic panel, liver function tests, and inflammatory markers, which of the following is the next best step in evaluation?

- A. Thiopurine methyltransferase test
- B. Interferon gamma release assay and hepatitis C antibody test
- C. Lipid panel
- D. Hepatitis B serologies and interferon gamma release assay
- E. No additional testing

CORRECT ANSWER: D

RATIONALE

Assessment for active and latent hepatitis B and tuberculosis should be performed in all patients with inflammatory bowel disease before initiation of anti-tumor necrosis factor (TNF) therapy. If there is active infection, it should be treated first in conjunction with infectious disease guidance on timing of anti-TNF therapy initiation. Latent infections may be treated concomitantly with anti-TNF therapy. There is no need to preemptively check a thiopurine methyltransferase on every patient with inflammatory bowel disease if you do not have the intention of initiating a thiopurine. Lipid monitoring is needed with tofacitinib therapy.

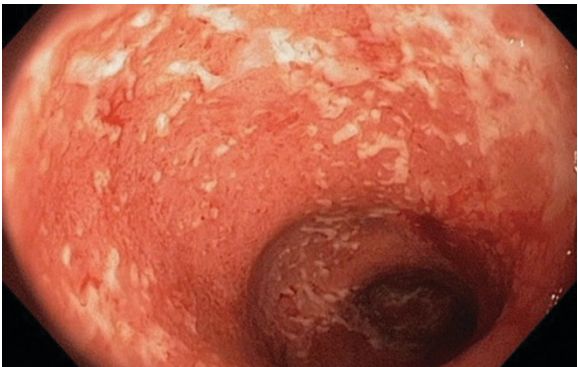
Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	2.9	3.5-5.5
C-reactive protein, mg/dL	60	≤0.8
Hemoglobin, blood, g/dL	8	Female: 12-16
Leukocyte count, cells/ μ L	14,000	4000-11,000
Platelet count, plt/μ L	473,000	150,000-450,000

REFERENCE
Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn’s Disease in Adults. *Am J Gastroenterol*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Question 6

The emergency department calls you for advice on a 40-year-old woman who presents for evaluation of bloody diarrhea. The emergency department doctor tells you that she has been having 4 months of bloody diarrhea up to 20 bowel movements (BMs) daily, including nocturnal BMs. She has significant nausea and abdominal pain and is not able to tolerate any oral intake; therefore, they are going to admit her to the hospital. They order a stool *Clostridium difficile* test, which is pending. Her laboratory test results are shown above.

You see her and arrange for a lower endoscopic evaluation the next day. This is what you see on the examination:



Rushed pathology confirms a diagnosis of ulcerative colitis (UC). You start her on intravenous methylprednisolone 20 mg every 8 hours. After 24 hours, she notes minor improvement, now report-

ing 15 BMs daily, but all still had blood in them. After 48 hours, she notes her abdominal pain improved from 10 to 9. After 72 hours of intravenous steroids, she remains with 15 bloody BMs daily and 8 or 9 on a scale of 10 in abdominal pain.

What is the next best step in management?

- A. Start infliximab
- B. Start tofacitinib
- C. Increase methylprednisolone to 100 mg intravenous three times daily
- D. Start ciprofloxacin and metronidazole
- E. Start vedolizumab

CORRECT ANSWER: A

RATIONALE
Patients who are hospitalized for severe acute UC and unresponsive to intravenous corticosteroid therapy should be treated with infliximab or cyclosporine. Tofacitinib may be used for the management of severe acute UC only after infliximab failure. Increasing corticosteroid dose will not result in significant benefit if an optimal dose was used initially. Antibiotics are not empirically indicated for the treatment of severe acute UC. Vedolizumab has a much slower onset of action and therefore is not appropriate for severe acute UC not responsive to intravenous corticosteroids.

REFERENCE
Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med*. 2013;369(8):699-710. doi:10.1056/NEJMoa1215734
Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of

Moderate to Severe Ulcerative Colitis. *Gastroenterology*. 2020;158(5):1450-1461. doi:10.1053/j.gastro.2020.01.006

Question 7

Your patient is a 36-year-old man with an 8-year history of pan ulcerative colitis who is most recently in clinical remission with adalimumab monotherapy and calls your office to report a flare of symptoms. He has had several ulcerative colitis flares in the past and feels that his current symptoms are quite characteristic of his typical flares. He was doing well until about 2 weeks before when he started experiencing an increase in bowel movements (BMs) from 2 formed BMs daily to 8 to 10 BMs daily, and he started seeing blood in his BMs. In the past, his flares were also responsive to prednisone. He does not like taking prednisone but is amenable to doing it if you recommend.

Which of the following do you recommend?

- A. Stool sample evaluation for fecal leukocytes
- B. Budesonide treatment instead of prednisone
- C. Stool sample evaluation to rule out *Clostridium difficile* infection
- D. Colonoscopy
- E. Evaluation by local emergency department

CORRECT ANSWER: C

RATIONALE

American Gastroenterological Association best practice advice is to rule out *Clostridium difficile* infection in patients presenting with a flare of inflammatory bowel disease. Fecal leukocytes could be checked, but they could be elevated in both inflammatory bowel disease flares as well as infections. Without evaluating for an active infection, it would not be prudent to simply treat for a flare. A colonoscopy is not the immediate next step in management. He is not reporting symptoms that raise alarm and need emergent evaluation as they are typical for him.

REFERENCE

Khanna S, Shin A, Kelly CP. Management of *Clostridium difficile* Infection in Inflammatory Bowel Disease: Expert Review from the Clinical Practice Updates Committee of the AGA Institute [published correction appears in Clin Gastroenterol Hepatol. 2017 Apr;15(4):607]. *Clin Gastroenterol Hepatol*. 2017;15(2):166-174. doi:10.1016/j.cgh.2016.10.024

Question 8

You are seeing a 55-year-old woman hospitalized for abdominal pain and bloody diarrhea. She receives a diagnosis of ulcerative colitis by colonoscopy and pathology upon admission. She is treated with intravenous steroids and received 1 dose of infliximab 10 mg/kg. After 3 days, she has no improvement in her symptoms and therefore receives a second dose of infliximab 10 mg/kg. The day after, her blood work is notable for a new anion gap. You request a lactate to be checked, which returns at 7.

What is the next best step in her management?

- A. Order magnetic resonance enterography
- B. Consult a colorectal surgeon
- C. Start intravenous cyclosporine
- D. Start ciprofloxacin and metronidazole
- E. Re-dose infliximab

CORRECT ANSWER: B

RATIONALE

In patients failing to adequately respond to medical therapy in 3 to 5 days, surgical consultation should be obtained. A magnetic resonance enterography is unlikely to change the diagnosis or prognosis at this time. Cyclosporine as rescue therapy for infliximab has been associated with serious adverse events, including death. Antibiotics are not indicated for the management of severe acute ulcerative colitis. Redosing infliximab after 2 doses is unlikely to result in any additional benefit.

REFERENCE

Maser EA, Deconda D, Lichtiger S, Ullman T, Present DH, Kornbluth A. Cyclosporine and infliximab as rescue therapy for each other in patients with steroid-refractory ulcerative colitis. *Clin Gastroenterol Hepatol*. 2008;6(10):1112-1116. doi:10.1016/j.cgh.2008.04.035

Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol*. 2019;114(3):384-413. doi:10.14309/ajg.0000000000000152

Question 9

You are called to consult on a 47-year-old woman in the emergency department with concern for severe acute ulcerative colitis. Laboratory test results are below.

Stool *Clostridium difficile* test is negative, and a computed tomography is notable for pancolitis. You recommend admission for an expedited endoscopic evaluation. Endoscopy and histology confirm a diagnosis of ulcerative colitis (UC). You recommend starting intravenous corticosteroids and monitoring stool frequency closely. The hospitalist has never managed a patient with UC before and asks if there are any other recommendations you have. What is the next step in management?

- A. Consult surgery, as this patient will need a colectomy
- B. Order serum perinuclear anti-neutrophil cytoplasmic antibody and anti-*Saccharomyces cerevisiae* antibody tests to confirm the diag-

- nosis of UC
- C. Start ciprofloxacin and metronidazole for the treatment of colitis
- D. Consult rheumatology, as patients with inflammatory bowel disease often have concomitant rheumatologic diagnoses
- E. Start prophylactic anticoagulation to prevent a venous thromboembolism

CORRECT ANSWER: E

RATIONALE

In patients with severe acute ulcerative colitis, deep vein thrombosis prophylaxis is strongly recommended, but often not provided because of concern for ongoing bleeding. However, the proinflammatory state creates a prothrombotic environment and these patients are at high risk for clotting. Since the patient has not even received a trial of intravenous corticosteroids, it would be premature to determine that the patient will need surgery, although surgical consultation can still be considered. Serologic testing to determine the diagnosis or prognosis for UC is not useful. Antibiotics are not indicated for the management of severe acute UC. Although patients with inflammatory bowel disease may often have concomitant rheumatologic diagnoses, this patient does not require immediate, in-hospital, rheumatologic evaluation based on the information provided.

REFERENCE

Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol*. 2019;114(3):384-413. doi:10.14309/ajg.0000000000000152

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.3	3.5-5.5
C-reactive protein, mg/dL	60	≤0.8
Erythrocyte sedimentation rate (Westergren), mm/hr	55	Female: 0-20
Hemoglobin, blood, g/dL	8	Female: 12-16
Platelet count, plt/μL	470,000	150,000-450,000

Question 10

You do a screening colonoscopy on a 58-year-old man with a history notable for hypertension and hyperlipidemia. During the colonoscopy, you note mild inflammation throughout the colon and biopsy it. After the colonoscopy, you discuss this with the patient who admits to having 4 to 5 loose bowel movements daily and blood in the stool about once or twice weekly, but he is not too bothered by it. In 4 days, you call the patient with the results of the pathology report, which state mild crypt-architectural distortion, features of chronicity, etc. What is the best course of treatment now?

- A. Mesalamine 875 mg twice daily
- B. Prednisone 10 mg daily
- C. Mesalamine 3600 mg daily
- D. Budesonide 6 mg daily
- E. No treatment

CORRECT ANSWER: C

RATIONALE

In patients with extensive mild to moderate ulcerative colitis, the American Gastroenterological Association recommends using standard-dose mesalamine (2-3 g daily) rather than low-dose mesalamine.

REFERENCE

Ko CW, Singh S, Feuerstein JD, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. *Gastroenterology*. 2019;156(3):748-764. doi:10.1053/j.gastro.2018.12.009

Question 11

A 33-year-old woman presents to your clinic for a second opinion on a new diagnosis of ulcerative proctitis (UP). She was having 3 loose bowel movements daily without any blood. She was prescribed mesalamine 2 g twice daily, but she cannot take pills and does not want to put medicine into her body systemically unless she had no other choice. She presents to your office because she

heard that steroids inserted through her rectum would be a good treatment. You tell her:

- A. Enemas are never indicated for induction of remission in UP
- B. Steroid enemas are the best topical treatment for UP
- C. Enemas should always be used for the management of UP
- D. Mesalamine enemas are the best topical treatment for UP

CORRECT ANSWER: D

RATIONALE

In patients with mild-to-moderate ulcerative proctitis who choose rectal therapy over oral therapy, the American Gastroenterological Association suggests using mesalamine enemas rather than rectal corticosteroids.

REFERENCE

Ko CW, Singh S, Feuerstein JD, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. *Gastroenterology*. 2019;156(3):748-764. doi:10.1053/j.gastro.2018.12.009

Question 12

A 29-year-old woman was diagnosed with moderate ulcerative pancolitis 1 year ago. She was prescribed vedolizumab shortly after diagnosis and achieved clinical remission in 6 months. You just performed a colonoscopy and noted endoscopic remission. You took random biopsies through the colon. During your follow-up office visit, you report to her that she has even achieved histologic remission. She asks you when her next colonoscopy should be.

Assuming she remains in remission, when should it be?

- A. Next year
- B. In 3 years

- C. In 5 years
- D. In 7 years
- E. In 10 years

CORRECT ANSWER: D

RATIONALE

If the patient is in endoscopic remission, there is no indication for routine colonoscopies until the first screening colonoscopy, which should begin after 8 to 10 years of diagnosis. Since the patient was diagnosed 1 year before this anecdote, 10 years would be 11 years after diagnosis and, hence, the incorrect answer.

REFERENCE

Ko CW, Singh S, Feuerstein JD, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. *Gastroenterology*. 2019;156(3):748-764. doi:10.1053/j.gastro.2018.12.009

Question 13

A 38-year-old forklift operator with a history notable for pan ulcerative colitis in clinical remission with sulfasalazine presents to you for routine follow-up. He has not had a visit in 1 year. You mention that you need to obtain blood work. He does not like being stuck and wants to know why blood work is needed since he had these tests 5 years ago and is generally healthy.

Which of the following do you explain as the reason for blood work?

- A. To adhere to routine practice and good form
- B. To check for medication side effects and screen for anemia
- C. To check for medication side effects and primary sclerosing cholangitis
- D. To check for medication side effects and screen for cancer

CORRECT ANSWER: C

RATIONALE

Patients with inflammatory bowel disease should be screened annually for primary sclerosing cholangitis and to evaluate for medication side effects. Although it is routine practice and good form, it is important to be intentional about testing patients and have indications for everything you do. Although checking for medication side effects and primary sclerosing cholangitis could be correct, it is not the only reason you obtain blood work. You should not be screening for cancer with blood work.

REFERENCE

Ko CW, Singh S, Feuerstein JD, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. *Gastroenterology*. 2019;156(3):748-764. doi:10.1053/j.gastro.2018.12.009

Question 14

A 73-year-old woman comes to your office for assessment of watery diarrhea. You perform a colonoscopy, which is completely normal. You take random biopsies, and pathology reports reveal lymphocytic colitis.

What should you recommend for this patient?

- A. Budesonide
- B. Bismuth
- C. Mesalamine
- D. Cholestyramine
- E. Symptom monitoring; treatment only if symptoms worsen

CORRECT ANSWER: A

RATIONALE

In patients with symptoms and pathology consistent with a microscopic colitis, budesonide is the first-line treatment and preferred over no treatment or the other treatment options. It is not reasonable to monitor her symptoms expectantly.

REFERENCE

Nguyen GC, Smalley WE, Vege SS, Carrasco-Labra A; Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on the Medical Management of Microscopic Colitis. *Gastroenterology*. 2016;150(1):242-e18. doi:10.1053/j.gastro.2015.11.008

Question 15

A 69-year-old woman presents for evaluation of 3 months of watery diarrhea. She has no significant medical problems but tore her anterior cruciate ligament while running about 6 months ago and required a hospitalization and orthopedic surgery. She recovered very well from the procedure, but 3 months ago she started noticing extremely loose bowel movements with significant urgency. She was having 2 to 3 such bowel movements daily. It is extremely distressing to her and causing her to be scared to leave her house.

What is the next best step in her management?

- A. Order a colonoscopy
- B. Prescribe mesalamine
- C. Order a flexible sigmoidoscopy
- D. Prescribe ciprofloxacin
- E. Review her medication list

CORRECT ANSWER: E

RATIONALE

Although a colonoscopy is a right answer, the immediate next step is to review the medication list in detail. In all patients, but especially older adults, medication lists should be carefully reviewed at every visit. For this patient, it should be reviewed to determine if she is treated with any of the medications more commonly associated with microscopic colitis. It would not be reasonable to prescribe her mesalamine without a diagnosis. A flexible sigmoidoscopy can be considered for the diagnosis of microscopic colitis, but if that is performed, biopsies from the descending colon should be done in addition to the rectosigmoid co-

lon. It is important to note that if the biopsies are unrevealing, the diagnosis of microscopic colitis is not ruled out because microscopic colitis can present with isolated right colonic involvement. Antibiotics are not indicated without a diagnosis.

REFERENCE

Nguyen GC, Smalley WE, Vege SS, Carrasco-Labra A; Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on the Medical Management of Microscopic Colitis. *Gastroenterology*. 2016;150(1):242-e18. doi:10.1053/j.gastro.2015.11.008

Question 16

A 29-year-old woman presents to your office for a second opinion on the management of inflammatory ileocolonic Crohn's disease. Her primary gastroenterologist prescribed infliximab, and she felt very well for 4 months with complete resolution of abdominal pain and normal bowel function. She is slowly starting to feel less well and did not have as robust a response after her last infusion. Therefore, she presents to discuss options to optimize infliximab with you. After an extensive conversation about her options, you advise adding methotrexate to infliximab.

You counsel her that:

- A. Methotrexate is relatively contraindicated in pregnancy
- B. There is no need for birth control while on methotrexate because methotrexate is an abortifacient
- C. Methotrexate is safe in pregnancy
- D. She should use 2 forms of birth control while taking methotrexate because methotrexate is a teratogen

CORRECT ANSWER: D

RATIONALE

Methotrexate is absolutely contraindicated in pregnancy and not simply a relative contraindica-

tion. Although methotrexate is an abortifacient, it also has significant potential for teratogenicity; therefore, birth control should be strongly advised.

REFERENCE

Herfarth HH, Kappelman MD, Long MD, Isaacs KL. Use of Methotrexate in the Treatment of Inflammatory Bowel Diseases. *Inflamm Bowel Dis*. 2016;22(1):224-233. doi:10.1097/MIB.0000000000000589

Question 17

A 32-year-old woman with a diagnosis of inflammatory ileocolonic Crohn's disease in clinical and endoscopic remission with adalimumab would like a second opinion. She wants to discuss her intention to start trying for her first pregnancy in the next few months. You advise her:

- A. Adalimumab crosses the placenta and may be unsafe in pregnancy; therefore, switch adalimumab to certolizumab
- B. Since she is in clinical and endoscopic remission and desires pregnancy; stop adalimumab
- C. Continue adalimumab; it is safer for her to take adalimumab than risk a flare during pregnancy
- D. Stop adalimumab and switch to mesalamine
- E. Continue adalimumab and add azathioprine since she is at high risk of flare during pregnancy

CORRECT ANSWER: C

RATIONALE

Data from a prospective registry of over 500 women who were pregnant and receiving biologic agents revealed that biologics, thiopurines, and combination therapy with biologic agents and thiopurines were not associated with increased adverse maternal or fetal outcomes at birth or in the first year of life. Switching biologics for another that does not cross the placenta is not recommended because there is always a risk of flaring during biologic transitions.

REFERENCE

Mahadevan U, Long MD, Kane SV, et al. Pregnancy and Neonatal Outcomes After Fetal Exposure to Biologics and Thiopurines Among Women With Inflammatory Bowel Disease. *Gastroenterology*. 2021;160(4):1131-1139. doi:10.1053/j.gastro.2020.11.038

Question 18

You meet a 40-year-old man with newly diagnosed inflammatory ileocolonic Crohn's disease. He is currently treated with mesalamine 4800 g daily. Although he is bothered by abdominal pain and some diarrhea intermittently, he says his gastrointestinal symptoms are not his most distressing symptom. His knee pain is quite bothersome. He describes a swollen knee that hurts so much that it limits how much he can walk. Lately it has been happening nearly every day. He asks you what to do about his joint pain. Which of the following to you recommend?

- A. Evaluation by primary care physician, as the joint pain is unrelated to inflammatory bowel disease
- B. Referral to physical therapy for possible osteoarthritis
- C. Referral to orthopedic surgeon for further evaluation and diagnosis
- D. Treatment of IBD, as the joint pain is likely due to poorly controlled inflammation from IBD
- E. Evaluation by rheumatologists for potential rheumatoid arthritis

CORRECT ANSWER: D

RATIONALE

Peripheral arthritis is common in patients with IBD and often parallels disease activity. Treating the IBD will often relieve the arthritis.

REFERENCE

Malaty HM, Lo GH, Hou JK. Characterization and prevalence of spondyloarthritis and peripheral arthritis among patients with inflam-

matory bowel disease. *Clin Exp Gastroenterol*. 2017;10:259-263. Published 2017 Sep 27. doi:10.2147/CEG.S136383

Question 19

Your 25-year-old patient with Crohn's colitis, which is well controlled on high-dose mesalamine, calls your office because she does not have a primary care provider and did not know who else to call. She reports waking up in the morning to find that her right eye was red, it did not get better through the day and by lunch, her eye started hurting and she needed to be in a dark room. She asks you what to do. Which of the following do you recommend?

- A. Elective evaluation by an eye doctor
- B. Application of cold packs on her eye to see if it improves throughout the day
- C. Evaluation at local emergency department
- D. Treatment with a prednisone taper for a potential inflammatory condition
- E. Treatment with prednisone for a potential allergic reaction to something

CORRECT ANSWER: C

RATIONALE

This patient likely has uveitis. Ocular inflammation can be an extra-intestinal manifestation of inflammatory bowel disease. Alarm symptoms of ocular inflammation can be remembered with the mnemonic, RSVP: Redness, Sensitivity to light, Vision changes, and Pain; patients may have one or many of these features. Alarm symptoms should prompt emergent evaluation to ensure that ocular pressure is not high. Elevated ocular pressure with ocular inflammation is a sight-threatening condition. If ocular pressure is normal and other ocular emergencies have been ruled out, outpatient follow up with an ophthalmologist is warranted.

REFERENCE

Biedermann L, Renz L, Fournier N, et al.

Uveitis manifestations in patients of the Swiss Inflammatory Bowel Disease Cohort Study. *Therap Adv Gastroenterol*. 2019;12:1756284819865142. Published 2019 Aug 13. doi:10.1177/1756284819865142

Question 20

You meet a 28-year-old man who is newly diagnosed with Crohn's disease. He presents to discuss medical therapy for Crohn's disease. As you are about to examine him, he reveals that he is worried about his right leg; he had a bee sting there 2 weeks ago, it never healed, and it is becoming more painful.

On examination, his knee looks like:



Which of the following is the next best step in management?

- A. Refer for allergy testing
- B. Start infliximab therapy
- C. Defer biologic therapy until the lesion is healed
- D. Refer to dermatology for biopsy of the lesion
- E. Start antibiotic therapy

CORRECT ANSWER: B

RATIONALE

When a lesion is consistent with erythema nodosum in a patient with active inflammatory bowel disease, a biopsy is not needed, but the patient should be reassured that it will most likely heal with the initiation of antiinflammatory therapy

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	160	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	50	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	45	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0

to treat the inflammatory bowel disease. With a classic presentation, there is no need for additional referral.

REFERENCE

Roth N, Biedermann L, Fournier N, et al. Occurrence of skin manifestations in patients of the Swiss Inflammatory Bowel Disease Cohort Study. *PLoS One*. 2019;14(1):e0210436. Published 2019 Jan 25. doi:10.1371/journal.pone.0210436

Question 21

You are seeing a 33-year-old man with inflammatory Crohn’s colitis in follow-up. His symptoms are well controlled with adalimumab monotherapy. Laboratory results reveal the following above.

You review his prior labs and note that the alkaline phosphatase level has hovered between 110-130 U/L for the last few checks over the past 2 years. You call him to convey that his liver function tests are slightly abnormal. Which of the following do you recommend to him as the next best step?

- A. Recheck liver function in 3 months
- B. Reduce alcohol intake and recheck liver function in 3 months
- C. Evaluation of bile ducts with magnetic resonance cholangiopancreatography
- D. Lose some weight and recheck liver function in 6 months
- E. Evaluate liver with abdominal computed tomography

CORRECT ANSWER: C

RATIONALE

Primary sclerosing cholangitis should be sus-

pected in patients with alkaline phosphatase elevations. Cholangiography is needed for diagnosis and magnetic resonance imaging is the most noninvasive method.

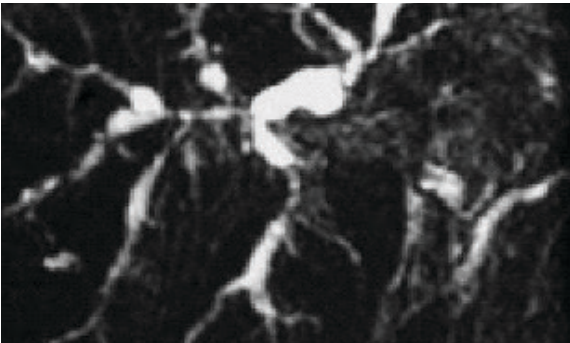
REFERENCE

Chapman R, Fevery J, Kalloo A, et al. Diagnosis and management of primary sclerosing cholangitis. *Hepatology*. 2010;51(2):660-678. doi:10.1002/hep.23294

Question 22

A 34-year-old woman with 3-year history of left-sided ulcerative colitis maintained with mesalamine presents to establish care with you after recently moving to the area. You learn that she has not had any other medical problems and has not had any surgeries. She has 1 well-formed bowel movement daily without any blood in her bowel movement, and she does not report any abdominal pain, joint pain, rashes, or any other symptoms. She has not had blood work checked in 2 years as she was busy with work and moving. She had a completely normal colonoscopy 2 years ago. You order laboratory tests and find that her alkaline phosphatase level is 250 U/L (reference range, 30-120 U/L), which is an isolated finding with no other liver function test (LFT) elevations. In reviewing her prior laboratory test results from 2 years ago, this is the first time she has had any abnormal LFTs. She does recall that when she was in college, she had blood drawn for a research study and she was told that 1 of her LFTs were abnormal.

You order a magnetic resonance cholangiopancreatography (MRCP) and find the following shown above right. You call her to convey the results and she asks you what to do next. You respond that you will do a colonoscopy and bone density test.



She shares that she really dislikes the preparation for colonoscopy and wonders how often she needs this procedure. You respond:

- A. Just once now and again in 5 years
- B. Every year
- C. Every 6 months
- D. Every 3 years
- E. It depends on what we find on this colonoscopy

CORRECT ANSWER: B

RATIONALE

Patients with primary sclerosing cholangitis are at especially high risk for colon dysplasia and cancer, so they should be screened at 1- to 2-year intervals.

REFERENCE

Chapman R, Fevery J, Kalloo A, et al. Diagnosis and management of primary sclerosing cholangitis. *Hepatology*. 2010;51(2):660-678. doi:10.1002/hep.23294

Question 23

A 52-year-old woman with a history notable for hypertension and hyperlipidemia and is undergoing treatment for lung cancer presents to you for evaluation of new-onset watery bowel movements, about 7 daily. She is having no abdominal pain, but the diarrhea is bothering her tremendously. She is not having any blood in her bowel movements, but she has lost 5 pounds since the diarrhea started. She has no recent travel or sick contacts. What is the next best step in evaluation?

- A. Flexible sigmoidoscopy
- B. Review of medications
- C. Stool testing for Giardia
- D. Loperamide treatment
- E. Abdominal computed tomography

CORRECT ANSWER: B

RATIONALE

Although a flexible sigmoidoscopy and stool testing for infections are reasonable steps, reviewing a patient's medication list to formulate a thorough differential diagnosis is very important. A diagnostic workup should be tailored to the differential diagnosis. Although loperamide could be recommended for symptomatic relief, attempts to make a diagnosis should be made concomitantly.

REFERENCE

Dougan M, Wang Y, Rubio-Tapia A, Lim JK. AGA Clinical Practice Update on Diagnosis and Management of Immune Checkpoint Inhibitor Colitis and Hepatitis: Expert Review. *Gastroenterology*. 2021;160(4):1384-1393. doi:10.1053/j.gastro.2020.08.063

Question 24

A 48-year-old woman with a recent diagnosis of metastatic breast cancer undergoing treatment with pembrolizumab presents for evaluation of diarrhea. She was doing well until she received her second dose of pembrolizumab, after which she developed sudden onset of 10 watery urgent bowel movements daily. Her oncologist empirically diagnosed a checkpoint inhibitor colitis and held the next 2 doses. She did note an improvement in her symptoms initially but feels that she cannot have fewer than 6 loose bowel movements daily with urgency. Therefore, she presents for evaluation at the recommendation of her oncologist. In addition to ordering blood work and stool studies, which of the following is the next best step?

- A. Abdominal computed tomography
- B. Prednisone

- C. Colonoscopy
- D. Infliximab
- E. Reassurance that the patient will continue to improve

CORRECT ANSWER: C

RATIONALE

Given persistent symptoms beyond Grade 1 toxicity (as defined by ≥ 4 bowel movements daily), the diagnosis should be confirmed with pathology. Other etiologies, such as microscopic colitis, should be ruled out. Empiric treatment with systemic corticosteroids would not be appropriate without confirming a diagnosis. Infliximab is indicated for checkpoint inhibitor colitis refractory to corticosteroid therapy.

REFERENCE

Dougan M, Wang Y, Rubio-Tapia A, Lim JK. AGA Clinical Practice Update on Diagnosis and Management of Immune Checkpoint Inhibitor Colitis and Hepatitis: Expert Review. *Gastroenterology*. 2021;160(4):1384-1393. doi:10.1053/j.gastro.2020.08.063

Question 25

You are asked to do a colonoscopy on a 72-year-old woman with new-onset diarrhea. You note in her chart that she has a history of atrial fibrillation, hyperlipidemia, gastroesophageal reflux disease, and arthritis. You perform colonoscopy and see:



Which of the following is most likely diagnosis?

- A. Ulcerative colitis
- B. Crohn's disease
- C. Drug-induced colitis
- D. Segmental colitis associated with diverticulosis
- E. Celiac disease

CORRECT ANSWER: D

RATIONALE

Although older adults presenting with diarrhea should be evaluated with a broad differential diagnosis, including inflammatory bowel diseases, recognizing classic endoscopic appearances is important to formulating a diagnosis.

REFERENCE

Ananthakrishnan AN, Nguyen GC, Bernstein CN. AGA Clinical Practice Update on Management of Inflammatory Bowel Disease in Elderly Patients: Expert Review. *Gastroenterology*. 2021;160(1):445-451. doi:10.1053/j.gastro.2020.08.060

Question 26

A 25-year-old woman developed bloody diarrhea, abdominal pain, and anemia. On examination, she is afebrile with moderate diffuse abdominal tenderness. Colonoscopy showed moderate-severe ileocolonic Crohn's disease (CD).

What is the most effective medicine for induction of remission in this patient?

- A. Azathioprine monotherapy
- B. Methotrexate monotherapy
- C. Infliximab monotherapy
- D. Tofacitinib and azathioprine
- E. Infliximab and azathioprine

CORRECT ANSWER: E

RATIONALE

In adults with moderate to severely active CD, combination therapy with infliximab and thiopurines is superior to azathioprine, methotrexate, or

infliximab monotherapy, for inducing remission. Tofacitinib is approved for ulcerative colitis but not CD.

REFERENCE

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 27

A 22-year-old man recently diagnosed with non-stricturing, noninflammatory ileocolonic Crohn's disease (CD) has been hospitalized and given intravenous steroids for moderate to severe symptoms at presentation. He was tapered off steroids with rapid recurrence of diarrhea and abdominal pain and was restarted on prednisone 40 mg daily. His diarrhea and pain are resolved on prednisone 40 mg daily.

Which of the following is the most appropriate time to start a tumor necrosis factor inhibitor (TNFi) in this patient?

- A. TNFi should be started now
- B. After failure of trial of 5-aminosalicylate
- C. After failure of trial of tofacitinib
- D. After failure of azathioprine monotherapy
- E. TNFi is contraindicated in this patient

CORRECT ANSWER: A

RATIONALE

In adult outpatients with moderate to severe CD, a top-down treatment strategy would be more effective than step therapy (escalation to biologic-based therapy only after failure of mesalamine and/or immunomodulators) for achieving remission and preventing disease-related complications. Treatment with 5-aminosalicylate is not effective for induction or maintenance of remission of CD. Tofacitinib is Food and Drug Administration

(FDA) approved for ulcerative colitis but not CD. The patient does not have any contraindications to anti-TNF.

REFERENCE

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 28

A 65-year-old woman with ileal Crohn's disease (CD) presents with diarrhea for 3 weeks. She has a remote history of intermittent prednisone for flare symptoms, but no treatment for over 3 years. She has a history of glaucoma and multiple sclerosis. On examination, she is afebrile with mild right lower quadrant tenderness. Colonoscopy shows active inflammation and ulceration in the terminal ileum.

What is the best next management option?

- A. Oral 5-aminosalicylate
- B. Oral prednisone
- C. Intravenous infliximab induction
- D. Intramuscular azathioprine
- E. Oral ileal release budesonide

CORRECT ANSWER: E

RATIONALE

In adult with moderate to severe CD involving the distal ileum, controlled ileal release budesonide is effective for inducing remission. It is important to note that budesonide has only been approved for short-term use. 5-aminosalicylate is not indicated for induction of remission for CD. Patient already has steroid-related complication of glaucoma so systemic steroids should be avoided. Patient has a demyelinating condition (multiple sclerosis) which is a contraindication to tumor necrosis factor inhibitor. Azathioprine is not given intramuscularly.

REFERENCE

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 29

A 33-year-old woman with ileal Crohn's disease, previously in remission on azathioprine monotherapy, presents with perianal tenderness and drainage. On examination, she is afebrile and has an actively draining perianal fistula without fluctuance or abscess.

What is the next best treatment?

- A. Increase azathioprine
- B. Add ustekinumab
- C. Add prednisone
- D. Add budesonide
- E. Diverting colostomy

CORRECT ANSWER: B

RATIONALE

In adults with symptomatic perianal Crohn's disease, ustekinumab may be effective for achieving fistula closure and maintaining fistula closure. Azathioprine dose change for perianal fistula has uncertain benefit and empiric escalation without therapeutic drug monitoring has uncertain benefit. Steroids (prednisone, budesonide) are not associated with fistula closure. Diverting colostomy is a consideration for severe or refractory perianal disease but should consider medical management at first presentation.

REFERENCE

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 30

A 21-year-old man with Crohn's disease (CD) being treated with adalimumab presents to his gastroenterologist with perianal pain and drainage. On examination, patient has a new perianal fistula. Patient has magnetic resonance imaging of the pelvis, which shows a perianal fistula without abscess.

What is the next best treatment option to add?

- A. Azathioprine
- B. Methotrexate
- C. Ustekinumab
- D. Prednisone
- E. Ciprofloxacin

CORRECT ANSWER: E

RATIONALE

In adults with symptomatic fistulizing CD without perianal abscess, combination of tumor necrosis factor inhibitor and antibiotics is probably more effective than tumor necrosis factor inhibitor alone for achieving fistula closure. Addition of azathioprine or methotrexate may be reasonable options for escalation of luminal CD management but addition of ciprofloxacin is a better option. Addition of ustekinumab to adalimumab is not routinely recommended. Steroids are not recommended for fistula closure.

REFERENCE

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 31

A 35-year-old man with ileocolonic stricturing Crohn's disease (CD) is admitted to the hospital for abdominal pain and bowel obstruction and undergoes small bowel resection. He has a history of

2 prior ileocecal resections for CD 3 years earlier. His only prior medical therapy was intermittent prednisone.

What is the most appropriate option for the patient now to decrease risk of recurrence of ileal stricture?

- A. Adalimumab
- B. Ileal release mesalamine
- C. Lactobacillus
- D. Budesonide
- E. Ciprofloxacin

CORRECT ANSWER: A

RATIONALE

The patient is high risk for recurrence due to multiple prior surgical resections. Adalimumab is an anti-tumor necrosis factor, which reduces recurrence of CD after resection. There is moderate evidence supporting the use of anti-tumor necrosis factor monotherapy over 5-aminosalicylate monotherapy and antibiotic monotherapy for reducing recurrence of CD. There is unclear benefit with the use of mesalamine, probiotics, or budesonide to prevent postoperative CD recurrence.

REFERENCE

Regueiro M, Velayos F, Greer JB, et al. American Gastroenterological Association Institute Technical Review on the Management of Crohn's Disease After Surgical Resection. *Gastroenterology*. 2017;152(1):277-295.e3. doi:10.1053/j.gastro.2016.10.039

Question 32

A 32-year-old woman with stricturing ileal Crohn's disease (CD) presents to her gastroenterologist after an ileocolonic resection for obstructive symptoms. This was her only bowel surgery for CD.

What is the most appropriate postoperative monitoring recommendation for recurrence of this patient's disease?

- A. Colonoscopy 6-12 months after surgery
- B. Fecal calprotectin every 3 months after surgery
- C. Assessment for recurrence of CD symptoms 6-12 months after surgery
- D. C-reactive protein every 3 months after surgery
- E. No specific monitoring required

CORRECT ANSWER: A

RATIONALE

Routine endoscopic monitoring 6 to 12 months after surgical resection, with endoscopy-guided treatment is recommended to decrease risk of recurrence of CD, regardless of early postoperative management. Endoscopic recurrence precedes clinical recurrence so waiting for symptomatic recurrence is too late. C-reactive protein is non-specific and is not appropriate alone as postoperative surveillance. Fecal calprotectin is not recommended alone for postoperative surveillance.

REFERENCE

Regueiro M, Velayos F, Greer JB, et al. American Gastroenterological Association Institute Technical Review on the Management of Crohn's Disease After Surgical Resection. *Gastroenterology*. 2017;152(1):277-295.e3. doi:10.1053/j.gastro.2016.10.039

Question 33

A 35-year-old man with Crohn's disease with history of recent ileocecal resection presents for follow-up to his gastroenterologist. He is taking infliximab 5 mg/kg every 8 weeks. Ileocolonoscopy at 6 months after his operation shows 3 ulcers in neo-terminal ileum. He is asymptomatic.

What is the best management decision at this time?

- A. Increase infliximab dose
- B. Change infliximab to ustekinumab
- C. Continue infliximab at current dose
- D. Add azathioprine
- E. Add ciprofloxacin

CORRECT ANSWER: C**RATIONALE**

Crohn's disease after an operation is assessed using the Rutgeerts score. Fewer than 5 ulcers (i1) is considered low risk for postoperative recurrence and continuation of current therapy is most appropriate. More than 5 ulcers would be classified as Rutgeerts i2 or greater and medical optimization would be recommended at that time.

REFERENCE

Regueiro M, Velayos F, Greer JB, et al. American Gastroenterological Association Institute Technical Review on the Management of Crohn's Disease After Surgical Resection. *Gastroenterology*. 2017;152(1):277-295.e3. doi:10.1053/j.gastro.2016.10.039

Question 34

A 51-year-old woman with ileocolonic Crohn's disease (CD) has a progressive ileal stricture that now requires surgical resection. She was diagnosed with CD at 40 years of age and has been in clinical remission with adalimumab for the past 10 years. Patient smokes cigarettes daily and drinks 3-4 alcoholic beverages daily. Patient has poorly controlled blood pressure.

Which of the following factors in this patient is most associated with an increased risk of postoperative CD recurrence in this patient?

- A. Hypertension
- B. Alcohol consumption
- C. Tobacco use
- D. Age at CD diagnosis
- E. Duration of Crohn's diagnosis

CORRECT ANSWER: C**RATIONALE**

Tobacco, younger age at diagnosis (<30 year of age), and prior CD surgery are high-risk factors for postoperative CD recurrence. Hypertension and

alcohol are not associated with risk of postoperative CD recurrence.

REFERENCE

Regueiro M, Velayos F, Greer JB, et al. American Gastroenterological Association Institute Technical Review on the Management of Crohn's Disease After Surgical Resection. *Gastroenterology*. 2017;152(1):277-295.e3. doi:10.1053/j.gastro.2016.10.039

Question 35

A 24-year-old woman diagnosed with ileocolonic CD 6 months ago presents to her gastroenterologist for follow-up. She was initially treated with prednisone with adequate clinical response, but her symptoms recurred after prednisone taper. She has now achieved remission with prednisone and azathioprine 4 weeks ago. She completed the prednisone taper and remains in clinical remission. What is the best next management step?

- A. Continue azathioprine monotherapy
- B. Taper azathioprine and monitor off medicine
- C. Add vedolizumab to azathioprine
- D. Add 5-aminosalicylate (5-ASA) to azathioprine
- E. Taper azathioprine and add 5-ASA

CORRECT ANSWER: A**RATIONALE**

The patient has steroid-induced remission. She has previously failed prednisone taper and should be maintained on steroid-sparing maintenance therapy. Azathioprine is an appropriate steroid-sparing maintenance therapy. If the patient is already in remission on azathioprine monotherapy there is little value in adding vedolizumab or 5-ASA therapy. 5-ASA is not recommended for maintenance of remission of CD.

REFERENCE

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and

Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 36

A 20-year-old man diagnosed with ileal Crohn's disease (CD) 3 months prior, presents to his gastroenterologist for follow-up. He initially declined medical treatment as symptoms resolved spontaneously. However, diarrhea and abdominal pain has recurred for 2 weeks that is disrupting his activities of daily living, and he is now requesting medical therapy. What is the best next monotherapy management recommendation for this patient?

- A. Azathioprine
- B. Methotrexate
- C. Mesalamine
- D. Budesonide
- E. Natalizumab

CORRECT ANSWER: D

RATIONALE

Azathioprine and methotrexate may be used for maintenance of remission but not for induction or remission for CD. Mesalamine is not indicated for induction or maintenance for CD. Natalizumab is associated with progressive multifocal leukoencephalopathy and is not considered a first-line therapy for CD. Budesonide is a reasonable option for induction of remission for CD, but not for maintenance.

REFERENCE

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 37

A 35-year-old woman with colonic Crohn's disease (CD) diagnosed 1 year ago presents to her gastroen-

terologist for follow-up. She is currently in clinical remission with infliximab (IFX) 5 mg/kg every 8 weeks; however, she has noted an increase in diarrhea consistently 2 weeks before each infusion.

What is the next best management step?

- A. Increase IFX dose to 10 mg/kg every 8 weeks
- B. Decrease IFX interval to 5 mg/kg every 4 weeks
- C. Check IFX drug level and antibodies to IFX
- D. Stop IFX and change to ustekinumab
- E. Start prednisone 40 mg daily

CORRECT ANSWER: C

RATIONALE

In patients with active inflammatory bowel disease treated with anti-tumor necrosis factor agents, reactive therapeutic drug monitoring with drug and antibody level is recommended over empiric drug escalation or switching of medications. Increasing IFX dose or decreasing intervals would be appropriate if therapeutic drug monitoring showed inadequate levels and no antibodies. Patient is currently in remission so adding prednisone is not appropriate.

REFERENCE

Vande Casteele N, Herfarth H, Katz J, Falck-Ytter Y, Singh S. American Gastroenterological Association Institute Technical Review on the Role of Therapeutic Drug Monitoring in the Management of Inflammatory Bowel Diseases. *Gastroenterology*. 2017;153(3):835-857.e6. doi:10.1053/j.gastro.2017.07.031

Question 38

A 24-year-old man with ulcerative colitis was previously in clinical remission with infliximab but developed loss of response related to antibody formation. He is concerned about loss of response related to immunogenicity with his next therapy.

Which of the medications is most likely to have loss of response related to immunogenicity?

- A. Golimumab
- B. Azathioprine
- C. Tofacitinib
- D. Ozanimod
- E. Methotrexate

CORRECT ANSWER: A

RATIONALE

Loss of response to inflammatory bowel disease therapy from immunogenicity is related to biologic medications. Biologics are unique in that the immune system may recognize the biologic medicine as nonself and cause a humoral or cell-mediated immune response with the formation of anti-drug antibodies. Azathioprine, tofacitinib, ozanimod, and methotrexate are not biologics and therefore not prone to immunogenicity.

REFERENCE

Vande Casteele N, Herfarth H, Katz J, Falck-Ytter Y, Singh S. American Gastroenterological Association Institute Technical Review on the Role of Therapeutic Drug Monitoring in the Management of Inflammatory Bowel Diseases. *Gastroenterology*. 2017;153(3):835-857.e6. doi:10.1053/j.gastro.2017.07.031

Question 39

A 31-year-old woman with ulcerative colitis with prior moderate to severe disease was prescribed infliximab (IFX) for induction and maintenance with clinical remission 2 years ago. She now complains of increasing diarrhea, pain, and bleeding consistently 2-3 weeks before infusion. IFX drug levels and antibody testing were performed showing adequate drug levels and no anti-drug antibodies. Colonoscopy showed Mayo 2 activity. Infectious workup is negative. What is the next best management option?

- A. Continue IFX at current dose and interval
- B. Increase IFX dose to 10 mg/kg every 8 weeks
- C. Stop IFX and change to adalimumab
- D. Stop IFX and change to ustekinumab

- E. Add prednisone 20 mg/d and repeat therapeutic drug monitoring in 4 weeks

CORRECT ANSWER: D

RATIONALE

The patient has a secondary loss of response to IFX with mechanistic failure and adequate drug levels and no antibodies. She has active disease on colonoscopy and active symptoms, so continuing current treatment is not appropriate. She already has adequate drug level so dose escalation is not appropriate. Adalimumab is also a tumor necrosis factor inhibitor (TNFi) so change to another TNFi (in-class) would be appropriate for immunogenic failure (low drug level, high anti-drug antibody) but not mechanistic failure. Adding prednisone and repeating therapeutic drug monitoring is unlikely to reverse mechanistic failure.

REFERENCE

Vande Casteele N, Herfarth H, Katz J, Falck-Ytter Y, Singh S. American Gastroenterological Association Institute Technical Review on the Role of Therapeutic Drug Monitoring in the Management of Inflammatory Bowel Diseases. *Gastroenterology*. 2017;153(3):835-857.e6. doi:10.1053/j.gastro.2017.07.031

Question 40

A 21-year-old man with ulcerative colitis in clinical remission with azathioprine monotherapy for 6 months presents to his gastroenterologist for follow-up. The patient has no new complaints and remains in clinical remission. Lab monitoring has been up to date and normal as of 3 months ago. Which of the following tests should be performed related to medication monitoring in this patient at this time?

- A. Interferon-gamma release assay
- B. Thiopurine methyltransferase
- C. Complete blood count with differential
- D. Lipid panel
- E. No additional lab testing needed at this time

CORRECT ANSWER: C**RATIONALE**

Patients receiving azathioprine should be monitored for lymphopenia with complete blood count with differential periodically. Screening for tuberculosis with an interferon-gamma release assay should be considered before starting immunosuppression. Thiopurine methyltransferase is recommended before initiating thiopurines to identify patients at high risk for leukopenia. Lipid panel is recommended for tofacitinib but not azathioprine.

REFERENCE

Vande Casteele N, Herfarth H, Katz J, Falck-Ytter Y, Singh S. American Gastroenterological Association Institute Technical Review on the Role of Therapeutic Drug Monitoring in the Management of Inflammatory Bowel Diseases. *Gastroenterology*. 2017;153(3):835-857.e6. doi:10.1053/j.gastro.2017.07.031

Question 41

A 24-year-old woman with ulcerative colitis has a clinical response to prednisone 40 mg daily and azathioprine 2 mg/kg. After prednisone taper, she has an increase in diarrhea and urgency. Fecal calprotectin is 250 ug/g and infectious workup is negative.

What is the best next management option?

- A. Resume prednisone to 20 mg daily for maintenance
- B. Increase azathioprine to 3 mg/kg
- C. Add ustekinumab
- D. Check 6-TGN and 6-MMP levels
- E. Check anti-drug antibodies

CORRECT ANSWER: D**RATIONALE**

In patients with inflammatory bowel disease treated with thiopurines for active inflammatory bowel disease-related symptoms, reactive therapeutic

drug monitoring is recommended over empiric changes in dose of medication. Therapeutic drug monitoring for thiopurines is measurement of thiopurine metabolites 6-TPN and 6-MMP. Thiopurines are not biologics and anti-drug antibodies are not routinely available.

REFERENCE

Vande Casteele N, Herfarth H, Katz J, Falck-Ytter Y, Singh S. American Gastroenterological Association Institute Technical Review on the Role of Therapeutic Drug Monitoring in the Management of Inflammatory Bowel Diseases. *Gastroenterology*. 2017;153(3):835-857.e6. doi:10.1053/j.gastro.2017.07.031

Question 42

A 35-year-old woman with colonic Crohn's disease presents to her gastroenterologist for follow-up for active moderate to severe symptoms. She is naïve to biologics and immunosuppressants and is amenable to starting therapy. She has a family history of lymphoma and is concerned about the risk of Crohn's disease medications and risk of lymphoma.

Which of the following medications would best address her safety concern?

- A. Adalimumab
- B. Infliximab
- C. Golimumab
- D. Azathioprine
- E. Vedolizumab

CORRECT ANSWER: E**RATIONALE**

Anti-tumor necrosis factor and thiopurines are associated with a small increased risk of lymphoma. Vedolizumab has not been associated with solid tumor or lymphoma risk.

REFERENCE

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the

Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 43

Which of the following medications is associated with progressive multifocal leukoencephalopathy (PML)?

- A. Infliximab
- B. Adalimumab
- C. Ustekinumab
- D. Tofacitinib
- E. Natalizumab

CORRECT ANSWER: E

RATIONALE

PML is associated with suppression of leukocytes across the blood brain barrier from natalizumab. PML has not been associated with tumor necrosis factor inhibitor or tofacitinib.

REFERENCE

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 44

A 20-year-old man with colonic Crohn's disease being treated with ustekinumab presents to his gastroenterologist with increase in cramping abdominal pain and fecal urgency for the past 2 weeks that resolves after bowel movement. On examination, he is afebrile with mild left lower quadrant tenderness without rebound tenderness. Preclinic blood work showed normal complete blood count. Colonoscopy 1 month later showed endoscopic remission. What is the next best management step?

- A. Increase ustekinumab dose
- B. Add prednisone
- C. Check fecal calprotectin
- D. Check colonoscopy
- E. Reassurance

CORRECT ANSWER: C

RATIONALE

Fecal calprotectin should be considered to help differentiate the presence of inflammatory bowel disease from irritable bowel syndrome. Calprotectin correlates with endoscopic activity. The patient's symptoms could be either related to inflammation or overlapping irritable bowel syndrome so empiric escalation of dose or steroids without assessment is not appropriate. Patient had a recent normal colonoscopy so noninvasive testing would be preferred. Reassurance without assessment of inflammation is not recommended.

REFERENCES

Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults [published correction appears in *Am J Gastroenterol*. 2018 Jul;113(7):1101]. *Am J Gastroenterol*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Singh S, Proctor D, Scott FI, Falck-Ytter Y, Feuerstein JD. AGA Technical Review on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. *Gastroenterology*. 2021;160(7):2512-2556.e9. doi:10.1053/j.gastro.2021.04.023

Question 45

A 42-year-old man recently diagnosed with Crohn's disease (CD) presents to his gastroenterologist with questions about medications that may be related to a flare of his CD. He has dyslipidemia, osteoarthritis, reflux, and hypertension. Which of the following medications is most associated with potential exacerbation of CD flare?

- A. Ibuprofen
- B. Omeprazole
- C. Metoprolol
- D. Lisinopril
- E. Simvastatin

CORRECT ANSWER: A**RATIONALE**

Nonsteroidal antiinflammatory drugs (NSAIDs) may exacerbate CD activity. Although some patients may tolerate NSAIDs without CD exacerbation, patients should be counseled regarding potential risk of flare related to NSAIDs and to avoid them if exacerbation is noted. The other medications have not been significantly associated with CD flares.

REFERENCE

Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults [published correction appears in *Am J Gastroenterol*. 2018 Jul;113(7):1101]. *Am J Gastroenterol*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Question 46

A 27-year-old woman with Crohn's disease recently induced into remission with prednisone is interested in starting azathioprine.

Which test is most relevant to complete before initiating azathioprine?

- A. Lipid panel
- B. Thiopurine methyltransferase (TPMT)
- C. Thiopurine metabolites (6TG, 6MMP)
- D. Anti-drug antibodies
- E. Computed tomography enterography

CORRECT ANSWER: B**RATIONALE**

A major side effect of thiopurines is leukopenia. TPMT testing should be performed before initial

use of azathioprine or 6-mercaptopurine to identify patients at high risk of severe leukopenia. Even in patients with normal TPMT, serial complete blood count monitoring is recommended. Lipid panel is recommended for patients starting tofacitinib.

REFERENCE

Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults [published correction appears in *Am J Gastroenterol*. 2018 Jul;113(7):1101]. *Am J Gastroenterol*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Question 47

A 22-year-old woman with colonic Crohn's disease (CD) previously in remission with vedolizumab presents with increase in diarrhea and abdominal pain after missing 2 infusions. She is having 10 bloody bowel movements daily. Patient has abdominal pain limiting oral food intake for 2 days. On examination, she is afebrile with diffuse moderate abdominal tenderness. Initial testing shows hemoglobin, 7.6 g/dL (reference range [female], 12-16 g/dL); negative stool study for *Clostridioides difficile*; and fecal calprotectin of 600 µg/g (reference range, <50 µg/g).

What is the next best management step?

- A. Resume vedolizumab
- B. Start sulfasalazine
- C. Start intravenous prednisone
- D. Start budesonide
- E. Emergent total colectomy

CORRECT ANSWER: C**RATIONALE**

Intravenous corticosteroids should be used to treat severe or fulminant CD. Patient has clinical presentation and lab findings consistent with CD flare, likely secondary to being off of vedolizumab. She has severe disease as defined by Truelove and Witts criteria with more than 6 stools daily,

frequent bloody bowel movements, and anemia (<75% normal).

REFERENCE

Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults [published correction appears in *Am J Gastroenterol*. 2018 Jul;113(7):1101]. *Am J Gastroenterol*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Question 48

A 25-year-old man with Crohn's disease previously in clinical remission with azathioprine monotherapy presents with perianal pain and purulent drainage. Patient is afebrile and has tenderness and fluctuance on rectal examination.

What is the next best management step?

- A. Start infliximab
- B. Add prednisone
- C. Examination under anesthesia
- D. Check fecal calprotectin
- E. Increase azathioprine dose

CORRECT ANSWER: C

RATIONALE

Recognition and drainage of abscesses (surgically or percutaneously) and examination under anesthesia should be undertaken before treatment of fistulizing Crohn's disease with anti-tumor necrosis factor agents or increase in immunosuppression. Fecal calprotectin can be useful to assess for inflammation, but drainage of the abscess should occur before testing.

REFERENCE

Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults [published correction appears in *Am J Gastroenterol*. 2018 Jul;113(7):1101]. *Am J Gastroenterol*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Question 49

A 40-year-old woman is referred for recent diagnosis of colonic Crohn's disease (CD). She has no prior bowel surgery for CD, just a history of perianal fistula, now resolved. She drinks moderate amounts of alcohol daily. Her father was diagnosed with colon cancer at 55 years of age.

Which of her features are most associated with high risk of progressive disease?

- A. Age at diagnosis
- B. Perianal fistula
- C. Alcohol consumption
- D. Family history
- E. Gender

CORRECT ANSWER: B

RATIONALE

Features that are associated with a high risk for progressive CD include young age at diagnosis, initial extensive bowel involvement, ileal or ileocolonic involvement, perianal/severe rectal disease, and presenting with a penetrating or stenosis disease phenotype. This patient has a history of perianal disease. Alcohol and gender are not associated with higher risk of progressive CD. Family history of colon cancer is not associated with higher risk of progressive CD.

REFERENCE

Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults [published correction appears in *Am J Gastroenterol*. 2018 Jul;113(7):1101]. *Am J Gastroenterol*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Question 50

A 29-year-old man with ileocolonic Crohn's disease (CD) recently diagnosed with ileocolonoscopy presents to his gastroenterologist for evaluation. His only symptoms are diarrhea and rectal bleeding.

Which is the most appropriate next test to perform to complete his CD diagnostic evaluation?

- A. Magnetic resonance enterography
- B. Esophagogastroduodenoscopy
- C. Examination under anesthesia
- D. Gastric emptying study
- E. Positron emission tomography

CORRECT ANSWER: A

RATIONALE

Small bowel imaging should be performed as part of the initial diagnostic workup for patients with CD. Esophagogastroduodenoscopy and examination under anesthesia may be indicated if the patient has specific symptoms of upper gastrointestinal or perianal disease. Gastric emptying study and positron emission tomography are not routinely part of initial CD evaluation.

REFERENCE

Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults [published correction appears in *Am J Gastroenterol*. 2018 Jul;113(7):1101]. *Am J Gastroenterol*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

CHAPTER 14

Gastrointestinal cancers

Seth Crockett, MD, MPH and Aimee Lee Lucas, MD, MS, AGAF

Question 1

You are asked to give a talk to your local community health clinic on gastrointestinal (GI) cancer. Specifically, the director of the clinic wants to ensure that the clinic's providers are aware of the most common GI cancers among their adult population. Rank the top 4 GI cancers in the US, from highest to lowest incidence (both sexes combined).

- A. Colorectal cancer, liver cancer, esophageal cancer, pancreatic cancer
- B. Colorectal cancer, pancreatic cancer, liver cancer, gastric cancer
- C. Colorectal cancer, esophageal cancer, gastric cancer, liver cancer
- D. Colorectal cancer, gastric cancer, small intestinal cancer, liver cancer

CORRECT ANSWER: B

RATIONALE

This question tests knowledge of epidemiology of GI cancers in the US, specifically the 4 most common cancers. Colorectal cancer is the most common GI cancer among both men and women, with roughly 149,000 new cases each year. Following colorectal cancer, pancreatic cancer (~60,000 new cases/year), cancer of the liver and intrahepatic bile ducts (mostly hepatocellular carcinoma, ~42,000 new cases/year), and gastric cancer (~26,000 new cases/year) round out the top 4 GI cancers with the highest incidence (Choice B). Esophageal cancer (~19,000 new cases/year), gallbladder/biliary

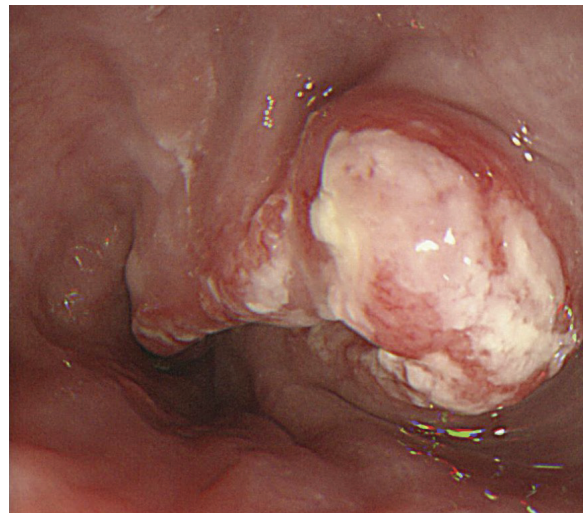
cancers (~12,000 new cases/year), and small intestinal cancers (~11,000 new cases/year) are less common.

REFERENCE

Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021 [published correction appears in *CA Cancer J Clin*. 2021 Jul;71(4):359]. *CA Cancer J Clin*. 2021;71(1):7-33. doi:10.3322/caac.21654

Question 2

A 65-year-old woman who emigrated from Malawi 5 years ago presents with problems swallowing certain foods and a gradual 10-pound weight loss. An upper endoscopy is performed showing the following lesion in the mid esophagus, which is biopsied. Which of the following is true regarding this diagnosis?



- A. Biopsies typically show glandular differentiation with underlying Barrett esophagus
- B. Potassium chloride, nonsteroidal antiinflammatory drugs, and bisphosphonates are frequent culprits
- C. Risk factors include consumption of hot beverages, tobacco and alcohol use, and diets low in fruit and vegetable intake
- D. Treatment with oral fluconazole is generally effective

CORRECT ANSWER: C

RATIONALE

This patient has esophageal squamous cell carcinoma (ESCC). Persons from sub-Saharan Africa (particularly countries of Eastern and Southern Africa) as well as of those from East and Central Asia are at higher risk of this cancer. In fact, Malawi, a country in Southeastern Africa, has the highest per-capita incidence of ESCC in the world. Other risk factors for ESCC include tobacco and alcohol use, consumption of high-temperature foods and beverages, certain nutritional deficiencies, and dietary nitrosamines (choice C). Men and women are equally affected with ESCC. Patients typically present with dysphagia as the presenting symptom. Tumors are frequently located in the mid esophagus, in contrast to esophageal adenocarcinoma (choice A), which typically affects the lower esophagus. Pill esophagitis and *Candida* esophagitis (choices B and D, respectively) typically present differently and have different endoscopic features compared with the lesion in the accompanying image.

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Abnet CC, Arnold M, Wei WQ. Epidemiology of Esophageal Squamous Cell Carcinoma. *Gastroenterology*. 2018;154(2):360-373. doi:10.1053/j.gastro.2017.08.023
 Arnold M, Soerjomataram I, Ferlay J, Forman D. Global incidence of oesophageal cancer by histological subtype in 2012. *Gut*. 2015;64(3):381-387. doi:10.1136/gutjnl-2014-308124

Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [published correction appears in *CA Cancer J Clin*. 2020 Jul;70(4):313]. *CA Cancer J Clin*. 2018;68(6):394-424. doi:10.3322/caac.21492

Question 3

A 68-year-old man with hypothyroidism and obesity presents with longstanding reflux symptoms and undergoes upper endoscopy, which demonstrates short-segment Barrett esophagus and *Helicobacter pylori* (*H pylori*) infection in the stomach. After *H pylori* eradication, he continues taking daily proton pump inhibitor (PPI) therapy for symptom control. One year later, he undergoes Roux-en-Y gastric bypass surgery for weight loss. Which of the following characteristics of this patient is associated with increased risk of developing esophageal adenocarcinoma (EAC)?

- A. Hypothyroidism
- B. Obesity
- C. *H pylori* infection
- D. Chronic PPI therapy
- E. Gastric bypass surgery

CORRECT ANSWER B

RATIONALE

In developed countries such as the US, EAC is more common than esophageal squamous cell carcinoma, and it is more common in men than women. The median age of presentation is 68 years, the same age as this patient. In addition to gastroesophageal reflux disease and Barrett esophagus, risk factors for EAC include age, white race (likely confounded by other determinants of health), male sex, obesity (particularly central obesity), and tobacco use. In contrast, *H pylori* infection is inversely related to both Barrett esophagus and EAC. Proton pump inhibitor use has been linked to lower risk of EAC, and PPIs are therefore recommended in guidelines for patients with Bar-

rett esophagus to prevent neoplastic progression. Similarly, Roux-en-Y gastric bypass reduces acid reflux, and there is evidence that this surgery decreases progression of Barrett esophagus. Hypothyroidism has not been linked to EAC.

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Question 4

A 36-year-old woman undergoes routine upper endoscopy to investigate bothersome reflux symptoms. She denies any dysphagia or weight loss. Upper endoscopy demonstrates a 5-mm extension of salmon-colored mucosa above the top of the gastric folds into the tubular esophagus. Biopsies of this area demonstrate the presence of columnar mucosa. Which of the following is true regarding her risk of esophageal cancer?

A. Her risk of esophageal cancer is low, and endoscopic surveillance is not indicated

- B. Biopsy results confirm the presence of short-segment Barrett esophagus and an accompanying elevated risk of esophageal cancer death
- C. Lifelong proton pump inhibitor therapy is indicated to reduce her risk of developing esophageal adenocarcinoma
- D. Repeat surveillance endoscopy should be performed in 3 years
- E. Radiofrequency ablation should be performed to eradicate the Barrett segment and reduce the risk of developing high-grade dysplasia and cancer

CORRECT ANSWER: A

RATIONALE

This patient has an irregular z-line, defined as columnar mucosa extending less than 1 cm proximal to the gastroesophageal junction. This condition is not associated with substantially elevated risk of esophageal adenocarcinoma. Her age and sex are also generally associated with lower risk of esophageal adenocarcinoma. Therefore, neither endoscopic surveillance nor proton pump inhibitor therapy (for chemoprevention alone) is necessary at this time.

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Question 5

Which of the following disorders are associated with increased risk of esophageal squamous cell carcinoma (ESCC)?

- A. Tylosis, Plummer-Vinson syndrome, and Fanconi anemia
- B. Gastroesophageal reflux, Schatzki ring, and hiatal hernia
- C. *Helicobacter pylori* infection, obesity, and dental caries
- D. History of congenital tracheoesophageal fistula, esophageal squamous papilloma, and esophagogastric junction outflow obstruction.

CORRECT ANSWER: A

RATIONALE

Certain esophageal diseases are known to increase the risk of ESCC, including tylosis (leukoplakia, hyperkeratosis, and esophageal papillomas), history of caustic ingestion (particularly lye), Plummer-Vinson syndrome (iron deficiency anemia and esophageal web formation), Fanconi anemia (an inherited bone marrow failure syndrome) achalasia, and systemic sclerosis. These associations, though rare, tend to be over-represented on board examination questions. In contrast, there is not an established relationship between ESCC and history of tracheoesophageal fistula, squamous papillomas, *Helicobacter pylori* infection, obesity, Schatzki ring, dental caries, esophagogastric junction outflow obstruction, or hiatal hernia.

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Question 6

A 75-year-old man is referred for an upper endoscopy by his primary care physician for bothersome heartburn. He has no other medical problems and takes no regular medications. His endoscopy demonstrates a segment of salmon-colored mucosa extending above the gastroesophageal junction, as well as a hiatal hernia. The diaphragmatic hiatus is located at 41 cm from the incisors, and the proximal extent of circumferential mucosal changes is

located at 31 cm from the incisors, with several tongues extending proximal to this. In addition, a 1-cm area of irregular raised mucosa is visualized in the distal esophagus. Which of the following is the best course of management?

- A. Documenting the presence of long-segment Barrett esophagus, with a length of 10 cm
- B. Random biopsies taken within the segment of salmon-colored mucosa, placed in a single jar
- C. Two biopsies every 1 cm of suspected Barrett mucosa
- D. Biopsy of the area of irregular raised mucosa submitted in a separate jar for pathology review
- E. Proceeding directly to radiofrequency ablation of the abnormal mucosa

CORRECT ANSWER: D

RATIONALE

Proper documentation of suspected Barrett esophagus includes use of Prague classification to document the maximal extent of any proximally extending tongues or islands of Barrett mucosa as well as the extent to circumferential changes, in relation to the gastroesophageal junction or top of the gastric folds (not the diaphragmatic hiatus). Four quadrant biopsies should be obtained every 2 cm, and any areas of irregular, raised, or depressed mucosa should be carefully described, biopsied separately, and placed in a separate jar in order to guide subsequent management. Proceeding directly to radiofrequency ablation before the diagnosis of Barrett esophagus (and degree of dysplasia, if any) is established histopathologically would not be appropriate.

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Sharma P, Katzka DA, Gupta N, et al. Quality indicators for the management of Barrett's esophagus, dysplasia, and esophageal adenocarcinoma: international consensus recommendations from the American Gastroenterological Association Symposium. *Gastroenterology*. 2015;149(6):1599-1606. doi:10.1053/j.gastro.2015.08.007

Question 7

Which of the following statements is true regarding epidemiology of hepatocellular carcinoma (HCC)?

- A. The prevalence of hepatitis C virus (HCV) correlates with HCC in most areas of the world
- B. Eighty-five percent of cases of HCC worldwide occur in sub-Saharan Africa and Asia
- C. HCC is the second most common cancer in the US, but has a low mortality rate
- D. In the US, most patients with HCC have alcohol-related liver disease

CORRECT ANSWER: B

RATIONALE

The vast majority of HCC cases occur in Asia and sub-Saharan Africa, largely correlated to high prevalence of hepatitis B (HBV) in these areas (not HCV). In the US, HCC is a relatively low incidence (~42,000 cases per year), but a high mortality (~30,000 deaths per year and 20% rate of 5-year survival). Most HCC cases in the US currently are related to HCV cirrhosis. However, it should be noted that HCC cases related to viral hepatitis are declining due to both vaccination (HBV) and effective therapies (HCV), although HCC related to nonalcoholic fatty liver disease is on the rise.

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Question 8

A 42-year-old man who immigrated to the US from Tanzania 10 years ago is referred to the gastroenterology clinic after testing positive for hepatitis B virus (HBV) by his primary care physician. The patient is asymptomatic. Laboratory testing reveals elevated HBV DNA, normal aminotransferase and bilirubin levels, and normal platelet count. A transient elastography test is done that is scored as Fo (no fibrosis). What would you recommend regarding screening in this patient?

- A. Initiate screening for hepatocellular carcinoma (HCC) starting at age 50
- B. Recommend upper endoscopy for varices screening now
- C. Abdominal ultrasound every 6 months
- D. Repeat transient elastography in 12 months
- E. Alpha fetoprotein now

CORRECT ANSWER: C

RATIONALE

Because of high incidence of HCC, largely owing to vertical transmission of HBV, HCC screening is recommended in African immigrant adults at the time of diagnosis, which includes patients like this man. Appropriate screening modalities include transabdominal ultrasound either alone or in combination with alpha fetoprotein level, but not alpha fetoprotein alone. Transient elastography is primarily used to assess liver fibrosis (absent in this case), and is not an established screening modality for HCC. Transient elastography can be helpful in some patients with liver disease to determine when cirrhosis has developed, and therefore when to initiate HCC screening. But this is not true of patients with HBV, who can develop HCC in the absence of cirrhosis. Screening for esophageal varices is not recommended in the absence of cirrhosis or portal hypertension.

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Question 9

Which of the following is true regarding the association between hepatitis B virus (HBV) and hepatocellular cancer (HCC)?

- A. Persistent HBV infection from vertical transmission increases the risk of HCC roughly 100-fold
- B. Only patients with HBV cirrhosis are at risk of HCC
- C. Level of HBV DNA does not correlate with risk of HCC
- D. Neither alcohol nor aflatoxin exposure potentiate risk of HCC in patients with chronic HBV
- E. Vaccination against HBV has not been shown to reduce the incidence of HCC

CORRECT ANSWER: A

RATIONALE

Vertical transmission of HBV is a strong risk factor for HCC, increasing the risk approximately 100-fold. Chronic HBV infection can also lead to HCC even in the absence of cirrhosis, and the degree of elevation in HBV DNA level has been shown to correlate with risk of HCC. Alcohol and aflatoxin exposure can further increase the risk of HCC in patients with chronic HBV. Universal

HBV vaccination is a proven method to reduce the incidence of HBV-associated HCC.

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El-Serag HB. Epidemiology of viral hepatitis and hepatocellular carcinoma. *Gastroenterology*. 2012;142(6):1264-1273.e1. doi:10.1053/j.gastro.2011.12.061

Question 10

A 67-year-old woman with type 2 diabetes, hypertension, obesity, and known nonalcoholic fatty liver disease (NAFLD) presents with new-onset abdominal swelling and discomfort. Laboratory studies reveal a normal complete blood count apart from low platelet count. Notable results are shown below.

She undergoes an abdominal ultrasound Doppler study that shows a shrunken liver with nodular contour, ascites, and splenomegaly. In addition, the ultrasound report indicates thrombosis of the portal vein, with a diameter of 25 mm.

What would be the most appropriate next step in management?

- A. Repeat ultrasound in 1 year
- B. Computed tomography abdomen with contrast

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.1	3.5-5.5
Aminotransferase, serum alanine (ALT, SGPT), U/L	55	10-40
Platelet count, PLT/ μ L	125,000	150,000-450,000

- C. Initiation of anticoagulation
- D. Referral for liver transplantation
- E. Referral for weight loss surgery

CORRECT ANSWER: B

RATIONALE

This patient has likely NAFLD cirrhosis based on laboratory findings and ultrasound features, which generally develops over decades. Yet, she has new-onset ascites, associated with a portal vein thrombosis. This should raise suspicion for hepatocellular cancer (HCC) in a patient with cirrhosis, especially with the finding of expansion of the portal vein. Computed tomography or magnetic resonance imaging, which are more sensitive for HCC than ultrasound (especially in obese patients) should be performed to exclude this possibility. Initiation of anticoagulation should be considered in patients with portal vein thrombosis, but exclusion of HCC would be higher priority in this case. Similarly, if tumor thrombus is present, this patient would not be a candidate for liver transplantation, so more diagnostic workup is needed before transplantation referral. Weight loss surgery can improve NAFLD outcomes in pre-cirrhotic patients but would not be appropriate in a patient with cirrhosis and portal hypertension due to increased risk of complications.

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Question 11

A 62-year-old man with a history of compensated hepatitis C cirrhosis undergoes a computed tomography that demonstrates a 5.5 cm lesion in the right lobe of the liver with arterial enhancement and portal venous washout. His total bilirubin level is 0.8 mg/dL (reference range, 0.3-1.0 mg/dL), platelet count is 225,000 (reference range, 150,000-450,000), and he has no ascites or known history of esophageal varices.

What is the most appropriate next step?

- A. Intravenous antibiotic therapy with piperacillin/tazobactam
- B. Referral for resection
- C. Referral for liver transplantation
- D. Sorafenib therapy

CORRECT ANSWER: B

RATIONALE

Imaging characteristics of the lesion in question are consistent with a hepatocellular cancer (HCC) that is larger than the maximum diameter allowed by Milan criteria for liver transplantation. Nevertheless, patients with healthy livers or compensated cirrhosis (no portal hypertension, normal bilirubin level) and a single lesion should be offered resection (ideally at an experienced center that can provide multidisciplinary liver care). Thus, chemotherapy would not be appropriate in this patient. The lesion does not have imaging characteristics of a liver abscess (nor are any signs of infection described in the stem), so antibiotics would also be inappropriate.

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lular carcinoma. *Liver Transpl.* 2004;10(2 Suppl 1):S115-S120. doi:10.1002/lt.20034

Question 12

A 59-year-old woman with a history of alcohol-related cirrhosis presents for her annual visit. She has a history of alcohol use disorder in remission, but is otherwise healthy, and her Model for End-Stage Liver Disease (MELD) score is 15. An abdominal ultrasound is ordered, which demonstrates multiple liver lesions suspicious for hepatocellular carcinoma (HCC). Magnetic resonance imaging (MRI) with contrast is performed, which confirms the presence of 3 distinct nodules measuring 1.8 cm, 2.4 cm, and 2.9 cm, with imaging features consistent with HCC.

What is the next most appropriate step in management?

- A. Systemic chemotherapy
- B. Radiofrequency ablation of all 3 lesions
- C. Repeat MRI in 6 months
- D. Referral for liver transplantation evaluation
- E. Supportive care

CORRECT ANSWER: D

RATIONALE

This patient has cirrhosis with a relatively low MELD score and develops multifocal HCC. However, lesions are below the threshold set forth by the Milan criteria (a single lesion <5 cm or up to 3 nodules <3 cm each) for determining eligibility for liver transplantation. Chemotherapy appears to be ineffective in this situation, and partial ablation would not be an appropriate strategy. Foregoing treatment would also not be appropriate given high risk of progression.

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Question 13

Which of the following is true regarding locoregional therapies for hepatocellular carcinoma (HCC)?

- A. Transarterial chemoembolization may reduce tumor burden and delay progression of intermediate stage HCC
- B. There is no risk of needle-tract seeding with radiofrequency ablation (RFA) of subcapsular tumors
- C. Percutaneous ethanol injection is preferred over RFA for tumors >2 cm
- D. Intratumoral injection of cyclophosphamide has been shown to prolong survival in patients with multifocal HCC
- E. Hepatic artery embolization improves survival in patients with advanced HCC and has an important role as a bridge to liver transplantation

CORRECT ANSWER: A

RATIONALE

Transarterial chemoembolization is an important modality, particularly for treatment of intermediate stage HCC. RFA also has a role, particularly for larger lesions, but does carry a risk of needle-tract seeding in up to 12% of patients. Percutaneous ethanol injection generally works better for smaller nodules, whereas RFA has a more predictable necrotic effect in tumors larger than 2 cm. Hepatic artery embolization may be offered as a palliative therapy but has not been shown to improve survival. Intratumoral injection of chemotherapeutics without embolization is not an established therapy for HCC, and cyclophosphamide is known to be associated with significant hepatotoxicity.

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Question 14

55-year-old woman undergoes her first screening colonoscopy at your facility. She has no family history of colorectal cancer. The bowel preparation is graded as Boston Bowel Preparation Score of 5, and a withdrawal time of 10 minutes is documented. No polyps are seen during her procedure, though sigmoid diverticulosis and melanosis coli were present.

Which of the following patient or procedure factors increase this patient's risk for future neoplasia?

- A. Female sex
- B. Bowel preparation
- C. Inadequate withdrawal time
- D. Presence of melanosis coli
- E. Sigmoid diverticulosis

CORRECT ANSWER: B

RATIONALE

This patient underwent screening colonoscopy with an adequate (>6 min) withdrawal time, but the bowel preparation was documented as suboptimal. Research shows that a total Boston Bowel Preparation Score lower than 6 (or segment score <2) is associated with a higher risk of future neoplasia. Neither melanosis coli nor diverticulosis are established risk factors for polyps or cancer, and men generally have higher risk of adenomatous polyps and cancer compared with women.

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Question 15

A 65-year-old woman undergoes surveillance colonoscopy, which identified a 3-mm lesion depicted in the photo below, located in the transverse colon. The lesion was completely removed using a cold snare. Her previous colonoscopy 5 years ago identified 1 to 2 diminutive polyps in the rectosigmoid colon that were read as hyperplastic.

Which of the following is an appropriate surveillance interval for this patient?



- A. 3 years
- B. 5 years
- C. 10 years
- D. Forego further surveillance given age

CORRECT ANSWER: C

RATIONALE

The lesion depicted in the image is a tubular adenoma, 3 mm in size per the description. Patients with 1 to 2 small (<10 mm) adenomatous polyps are at low risk of metachronous neoplasia, and they should be offered surveillance every 7 to 10 years. Arguably, a 10-year surveillance examination would be most appropriate for a patient with a single diminutive adenoma who has no family history of colorectal cancer and who had a previous colonoscopy without precancerous polyps. Though previous guidelines allowed for a 5-year surveillance interval for 1 to 2 small adenomas, current evidence (and guidelines) indicates 5 years would be overly aggressive. However, foregoing future surveillance would not be appropriate as this patient would still be within screening age in 10 years.

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Question 16

A 50-year-old patient undergoes their first screening colonoscopy. The bowel preparation is determined to be adequate. The examination identifies the lesion depicted below located in the sigmoid colon, estimated to measure 5 mm in diameter.



What is the best choice for polypectomy?

- A. Hot snare polypectomy
- B. Endoscopic mucosal resection
- C. Hot biopsy forceps polypectomy
- D. Cold biopsy forceps polypectomy
- E. Cold snare polypectomy

CORRECT ANSWER: E

RATIONALE

The lesion depicted is a small sessile adenomatous polyp. There are no features to suggest an invasive neoplasm. The best choice for resection would be cold snare polypectomy, which is associated with both a higher rate of complete resection compared with biopsy forceps techniques, and a lower risk of post-polypectomy bleeding compared with hot snare polypectomy. Endoscopic mucosal resection is generally not necessary for Paris class Is lesions smaller than 1 cm.

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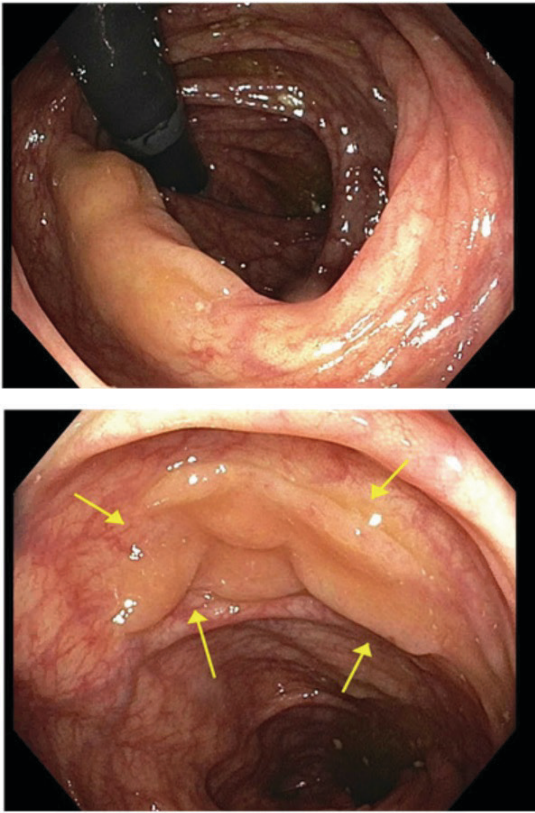
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Question 17

A 55-year-old woman undergoes her first lifetime colonoscopy. She is asymptomatic, and she has no family history of colorectal cancer. Her colonoscopy reveals 5 large flat polyps throughout her colon including two 30-mm lesions in the ascending and transverse colon, and several

smaller sessile polyps. Images of two of the larger polyps are shown below.



Which of the following is true of this patient?

- A. Colonoscopy should be repeated every 3-5 years
- B. She harbors a germline *BRAF* mutation
- C. Histologically, lesions are characterized by pencillate dark nuclei and pseudostratification
- D. She has an increased risk of several extraintestinal cancers including thyroid and ovarian cancer
- E. Close colonoscopic surveillance can mitigate risk of colorectal cancer

CORRECT ANSWER: E

RATIONALE

This patient meets criteria for serrated polyposis syndrome (SPS). WHO criteria for SPS include at least 5 serrated lesions or polyps proximal

to the rectum, all 5 mm or larger, with 2 or more that are 10 mm or larger, or more than 20 serrated lesions or polyps of any size distributed throughout the large bowel, with at least 5 proximal to the rectum. In contrast to most other polyposis syndromes, SPS represents an oligopolyposis for which there is no known germline mutation. Thus, although *BRAF* mutation is an important step in the serrated pathway, this does not occur at the germline level. SPS is also not associated with increased risk of extraintestinal malignancies. Histologically, serrated polyps are characterized by crypt serration and dilation and branching of crypt bases, not hyperchromatic nuclei and pseudostratification, which are features of tubular adenomas. The most effective strategy for reducing risk of colorectal cancer in patients with SPS involves close colonoscopic surveillance.

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Nagtegaal ID, Odze RD, Klimstra D, et al. The 2019 WHO classification of tumours of the digestive system. *Histopathology*. 2020;76(2):182-188. doi:10.1111/his.13975

Question 18

Which of the following is true regarding sporadically occurring adenomatous colorectal polyps?

- A. Only a minority of adenomatous polyps progress to cancer
- B. The transition from small tubular adenoma to cancer typically occurs in less than 10 years
- C. Villous adenomas typically progress to aberrant crypt foci, then to carcinoma in situ
- D. Invasive cancer develops quickly once low-grade dysplasia occurs in adenomatous polyps

- E. Subtypes of tubular adenomas include traditional serrated adenomas and sessile serrated adenomas

CORRECT ANSWER: A

RATIONALE

Only a minority of adenomas progress to cancer; the remainder are thought to grow indolently or regress. For those that are destined for cancer, the adenoma-carcinoma sequence typically occurs over 1 to 2 decades or more. Aberrant crypt foci (ACF) are thought to be the initial step before discrete tubular adenomas form (thus it is inaccurate that villous adenomas progress to ACF). All conventional adenomas harbor low-grade dysplasia by definition, so although high-grade dysplasia occurs in advanced lesions with a relatively high risk of progressing to cancer, the same is not true of low-grade dysplasia. Traditional serrated adenomas and sessile serrated adenomas (also known as sessile serrated lesions or polyps) are serrated class lesions that are histologically and etiologically distinct compared with tubular adenomas.

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Question 19

A 60-year-old woman undergoes fecal immunochemical test (FIT)-stool DNA testing (Colo-guard®), and the result is positive. She has no family history of colorectal cancer, and she denies any gastrointestinal symptoms. Her primary care physician orders a colonoscopy to be done in your facility.

What is the approximate likelihood that this patient will have a cancer on her colonoscopy?

- A. 5%
- B. 15%
- C. 25%
- D. 50%

CORRECT ANSWER: A

RATIONALE

This patient is at average risk of colorectal cancer based on the history given. As per epidemiologic studies, her pretest probability of having cancer is roughly 0.5% to 0.7%. Given the sensitivity and specificity of FIT-stool DNA of 92% and 87%, respectively, the posttest probability in this scenario would be roughly 5% (ie, 95% of patients will not have cancer).

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Question 20

A 40-year-old man is referred to gastrointestinal clinic for discussion of colorectal cancer (CRC) screening. He has never had a colonoscopy. He reports that his uncle was diagnosed with rectal cancer at 75 years of age but has no other family members with CRC. He has an older brother who recently underwent a screening colonoscopy that showed 2 small adenomatous polyps.

What would you recommend regarding CRC screening based on current guidelines?

- A. First colonoscopy now, subsequent follow-up per guidelines for average risk individuals
- B. First colonoscopy now, followed by surveillance every 5 years
- C. Initiate colonoscopy screening at age 50, followed by surveillance every 5 years
- D. Initiate average risk screening at age 45 by colonoscopy, fecal immunochemical test (FIT), or FIT-stool DNA

CORRECT ANSWER: D

RATIONALE

Initiating average risk screening at age 45 by either colonoscopy, FIT, or FIT-stool DNA is the best answer. Having a single second-degree relative with CRC diagnosed after age 60 does not appreciably increase one's risk of CRC, nor does having a first-degree relative with small polyps. Therefore, early initiation of screening is not needed, and he should follow guidelines for average risk individuals with respect to both age of initiation and surveillance intervals. In 2021, the

US Preventive Services Task Force began recommending the initiation of CRC screening at age 45 by various methods including colonoscopy, FIT, FIT-stool DNA, high-sensitivity guaiac-based fecal occult blood test (gFOBT), computed tomography colonography, or flexible sigmoidoscopy. FIT offers improved sensitivity for both advanced adenomas and cancers compared with gFOBT, and colonoscopy is generally preferred over sigmoidoscopy in the US given ability to detect and remove proximal lesions. Computed tomography colonography is also a screening option, though it has a lower sensitivity for both polyps and cancer compared with colonoscopy, and it is not widely available in the US.

REFERENCES

Gupta S, Lieberman D, Anderson JC, et al. Recommendations for Follow-Up After Colonoscopy and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology*. 2020;158(4):1131-1153.e5. doi:10.1053/j.gastro.2019.10.026

Rex DK, Boland CR, Dominitz JA, et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients From the U.S. Multi-Society Task Force on Colorectal Cancer. *Gastroenterology*. 2017;153(1):307-323. doi:10.1053/j.gastro.2017.05.013

US Preventive Services Task Force, Davidson KW, Barry MJ, et al. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2021;325(19):1965-1977. doi:10.1001/jama.2021.6238

Question 21

A 32-year-old woman undergoes her first lifetime colonoscopy for new-onset iron deficiency anemia and intermittent blood in stool. She is otherwise asymptomatic. Colonoscopy demonstrates over 200 sessile and pedunculated polyps scattered throughout the colon including a few larger than 10 mm. Several of the larger polyps were biopsied

and found to be tubular adenomas. What is the next most appropriate step for this patient?

- A. Repeat colonoscopy now with resection of larger polyps
- B. Take a careful family history to determine if she meets Amsterdam criteria
- C. Referral for genetic testing and colectomy
- D. Initiation of sulindac and celecoxib therapy

CORRECT ANSWER: C

RATIONALE

This patient has a polyposis phenotype, consistent with familial adenomatous polyposis, or (less likely given high number of polyps described), *MUTYH*-associated polyposis. Based on clinical presentation alone of a woman in her 30s with adenomatous polyposis, regardless of family history, genetic testing and counseling is warranted to determine if she carries a germline mutation in *APC*, and if cascade testing of other family members may be worthwhile. Given essentially 100% lifetime risk of colorectal cancer associated with familial adenomatous polyposis (FAP), prophylactic colectomy must be considered in order to prevent the occurrence of cancer and cancer death. Colonoscopy with polypectomy is generally unsuccessful with the degree of polyposis described in this patient. Amsterdam criteria applies to Lynch syndrome, not FAP. Both sulindac and celecoxib have been shown to have chemopreventive effects in FAP but would be premature at this point before a genetic diagnosis is established.

REFERENCE

Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol*. 2015;110(2):223-263. doi:10.1038/ajg.2014.435

Question 22

Which of the following is true regarding *MUTYH*-associated polyposis (MAP)?

- A. MAP is generally characterized by oligopolyposis (3-100 adenomas)
- B. MAP is transmitted in an autosomal dominant fashion
- C. In contrast to patients with familial adenomatous polyposis (FAP), patients with MAP do not have an increased risk of duodenal cancer
- D. MAP patients usually develop polyps at an earlier age compared with patients with FAP

CORRECT ANSWER: A

RATIONALE

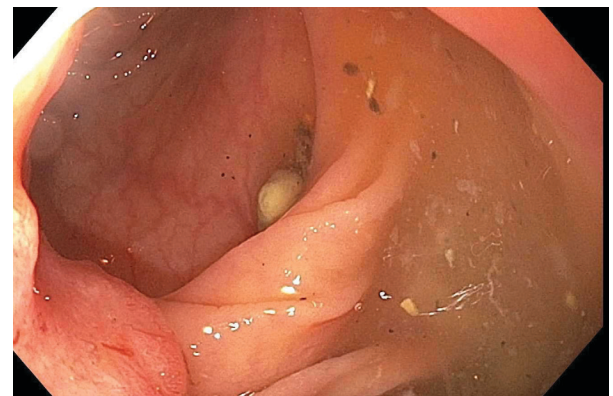
Patients with MAP generally exhibit an oligopolyposis, with 3 to 100 adenomas. Patients with MAP do have a risk of duodenal cancer, like patients with FAP. However, in contrast to FAP, MAP is transmitted in an autosomal-recessive manner, and patients with MAP develop polyps and cancer later (eg, 19% risk of colorectal cancer at age 50).

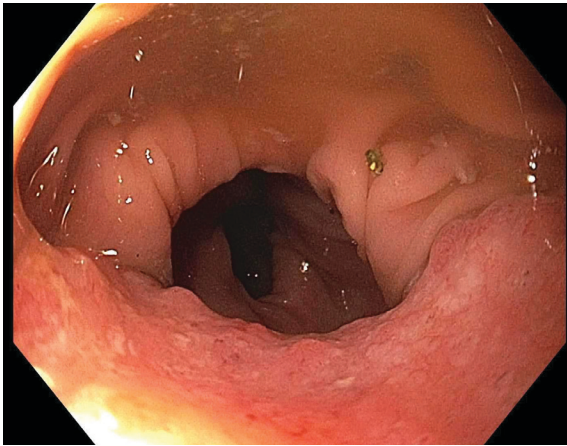
REFERENCE

Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol*. 2015;110(2):223-263. doi:10.1038/ajg.2014.435

Question 23

A 58-year-old man undergoes surveillance colonoscopy, which identifies the lesion depicted below in the sigmoid colon. The lesion is estimated to be 3 cm in diameter with a central depression





(Paris class Is + IIa). The area in the center of the lesion, when examined with narrow-band imaging, exhibits an amorphous surface pattern with areas of disrupted vessels.

What is the next best step in management?

- A. Removal of the lesion with endoscopic mucosal resection followed by tattoo placement distal to the lesion for future localization
- B. Biopsy of the edge of the lesion with management dependent on pathology results
- C. Biopsy of the center of the lesion and referral for surgical resection
- D. Removal of the lesion with standard hot snare polypectomy

CORRECT ANSWER: C

RATIONALE The lesion depicted is a small invasive cancer, characterized by central depression, narrow-band imaging characteristics suggestive of deep submucosal cancer based on the National Institute for Health and Care Excellence (NICE) criteria. Given these high-risk features, endoscopic mucosal resection would not be appropriate given increased risks, and lower likelihood of cure compared with surgical resection. The lesion should be carefully biopsied in the center, where histologic evidence of cancer is more likely, and the patient should be referred for oncologic resection. Biopsies from the edge of the lesion are more likely to result in sampling error and may lead to inappropriate management.

REFERENCES

Hewett DG, Kaltenbach T, Sano Y, et al. Validation of a simple classification system for endoscopic diagnosis of small colorectal polyps using narrow-band imaging. *Gastroenterology*. 2012;143(3):599-607.e1. doi:10.1053/j.gastro.2012.05.006

Shaukat A, Kaltenbach T, Dominitz JA, et al. Endoscopic Recognition and Management Strategies for Malignant Colorectal Polyps: Recommendations of the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology*. 2020;159(5):1916-1934.e2. doi:10.1053/j.gastro.2020.08.050

Question 24

A 40-year-old woman undergoes a partial colectomy for sigmoid colon cancer. She has a strong family history of colorectal cancer (CRC) in several first- and second-degree relatives. Her tumor is found to be microsatellite unstable. She subsequently undergoes genetic testing, which identifies a germline mutation in *MSH2* gene.

Which of the following is true of her condition?

- A. It is transmitted in an autosomal-recessive fashion
- B. It is associated with an increased risk of esophageal and parathyroid cancer
- C. She should be screened for endometrial cancer starting now
- D. Her risk of future CRC is minimal after surgery
- E. She has a lower risk of colon cancer compared with patients with *PMS2* mutations

CORRECT ANSWER: C

RATIONALE

This patient has Lynch syndrome, characterized by autosomal dominant inheritance, early-onset CRC, a microsatellite instability-high tumor, and germline testing that confirms a mutation in one of the mismatch repair genes: *MSH2*. Women with

Lynch syndrome are at substantially increased risk of endometrial cancer, and thus screening is recommended starting at age 30; therefore, screening should be initiated now in this patient. Lynch syndrome is associated with several other extraintestinal cancers including ovarian, kidney, ureter, bladder, stomach, small intestine, and glioblastoma, but is not associated with an increased risk of either esophageal or parathyroid cancer. Despite a partial colectomy, this patient is still at substantial increased risk of metachronous CRC in her remaining colon. *PMS2* mutation in Lynch syndrome is associated with a lower risk of both CRC and endometrial cancer.

REFERENCE

Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol*. 2015;110(2):223-263. doi:10.1038/ajg.2014.435

Question 25

A 52-year-old woman undergoes a screening colonoscopy. She has no chronic medical issues, does not smoke or drink alcohol regularly. She eats a protein-rich diet high in fish, meat, and dairy and low in carbohydrates. Her brother has Crohn's disease, but she has no family history of colorectal cancer (CRC). She takes 81mg aspirin daily. During her procedure, 5 suspected adenomatous polyps are removed including 2 larger polyps measuring 10 mm and 15 mm.

Which of the following factors are associated with increased risk of colorectal neoplasia?

- A. Female sex
- B. Diet high in fish
- C. Diet high in red meat and processed meat
- D. Diet high in dairy
- E. Family history of Crohn's disease
- F. Aspirin use

CORRECT ANSWER: C

RATIONALE

Male (not female) sex is an established risk factor for colorectal neoplasia. Red meat intake is also an established risk factor for CRC, but diets high in fish, calcium, dairy, vitamin D, and fruits/vegetables are associated with a lower risk of CRC. Aspirin and nonsteroidal antiinflammatory drug use are also associated with decreased risk of CRC. Having a family history of inflammatory bowel disease does not increase one's risk of CRC.

REFERENCES

American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022. Atlanta: American Cancer Society; 2020.

Chao A, Thun MJ, Connell CJ, et al. Meat consumption and risk of colorectal cancer. *JAMA*. 2005;293(2):172-182. doi:10.1001/jama.293.2.172

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Rock CL, Thomson C, Gansler T, et al. American Cancer Society guideline for diet and physical activity for cancer prevention. *CA Cancer J Clin*. 2020;70(4):245-271. doi:10.3322/caac.21591

Question 26

Which of the following statements regarding risk factors for colorectal cancer (CRC) is correct?

- A. Alaskan Native people have a higher risk of CRC than most other racial and ethnic groups
- B. Patients with ileal Crohn's disease have an elevated risk of CRC and should undergo more frequent colonoscopic surveillance than average risk persons
- C. Patients with acromegaly exhibit an increased risk of squamous cell cancer of the colon
- D. Patients with a history of ureterosigmoidostomy exhibit an increased risk of proximal CRC

CORRECT ANSWER: A

RATIONALE

Alaskan Natives have roughly twice the incidence of CRC compared with other racial and ethnic groups, for reasons that are not entirely clear. Although colitis associated with inflammatory bowel disease is a risk factor for CRC, Ileal Crohn's disease without colonic involvement does not appreciably increase one's risk of CRC. Thus, surveillance is only recommended for patients with Crohn's colitis that affects at least 30% of the colon. Acromegaly is associated with an increased risk of adenocarcinoma of the colon (not squamous cell carcinoma), and a history of ureterosigmoidostomy (a bladder cancer surgery now performed rarely) increases the risk of distal (not proximal) polyps and cancer.

REFERENCES

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Azimuddin K, Khubchandani IT, Stasik JJ, Rosen L, Riether RD. Neoplasia after ureterosigmoidostomy. *Dis Colon Rectum*. 1999;42(12):1632-1638. doi:10.1007/BF02236220

Dal J, Leisner MZ, Hermansen K, et al. Cancer Incidence in Patients With Acromegaly: A Cohort Study and Meta-Analysis of the Literature. *J Clin Endocrinol Metab*. 2018;103(6):2182-2188. doi:10.1210/jc.2017-02457

Ekbom A, Helmick C, Zack M, Adami HO. Increased risk of large-bowel cancer in Crohn's disease with colonic involvement. *Lancet*. 1990;336(8711):357-359. doi:10.1016/0140-6736(90)91889-i

Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Question 26

A 55-year-old man undergoes upper endoscopy for gastroesophageal reflux disease (GERD) despite twice-daily proton pump inhibitors (PPI) use. He is found to have a duodenal ulcer.

Which if the following *Helicobacter pylori* (*H pylori*) virulence factors is likely associated with duodenal ulcers and premalignant lesions of the stomach?

- A. *iceA*
- B. *EspP*
- C. *CagA*
- D. *VacA*
- E. Urease

CORRECT ANSWER: C

RATIONALE

The *CagA* virulence factor is noted in up to 85% of duodenal ulcers. It is also associated with gastric cancer and premalignant lesions of the stomach. *iceA* has been associated with peptic ulcers, while *VacA* leads to a strong inflammatory response. Urease is an enzyme produced by *H pylori* to allow it to survive in the acidic gastric environment and adhere to epithelial cells and *EspP* is an *Escherichia coli* virulence factor.

REFERENCES

Amieva M, Peek RM Jr. Pathobiology of Helicobacter pylori-Induced Gastric Cancer. *Gastroenterology*. 2016;150(1):64-78. doi:10.1053/j.gastro.2015.09.004

Fallone CA, Barkun AN, Göttke MU, et al. Association of Helicobacter pylori genotype with gastroesophageal reflux disease and other upper gastrointestinal diseases. *Am J Gastroenterol*. 2000;95(3):659-669. doi:10.1111/j.1572-0241.2000.01970.x

Weel JF, van der Hulst RW, Gerrits Y, et al. The interrelationship between cytotoxin-associated gene A, vacuolating cytotoxin, and

Helicobacter pylori-related diseases. *J Infect Dis.* 1996;173(5):1171-1175. doi:10.1093/infdis/173.5.1171

Question 27

A 70-year-old woman undergoes upper endoscopy for weight loss and epigastric pain. Endoscopic evaluation reveals a 2-cm gastric ulcer, and biopsies reveal gastric adenocarcinoma. Which if the following is a risk factor for gastric cancer?

- A. Variant of uncertain significance in *E-cadherin*
- B. Peutz-Jeghers syndrome
- C. Fundic gland polyps
- D. Selenium exposure
- E. Whipple's disease

CORRECT ANSWER: B

RATIONALE

Helicobacter pylori is the most important risk factor for gastric cancer worldwide. Although a pathogenic or likely pathogenic variant in *E-cadherin* is associated with gastric cancer, no increased risk is typically found with a variant of uncertain significance. Other hereditary risk factors for gastric cancer include Peutz-Jeghers syndrome (*STK11*) and Lynch syndrome. Although fundic gland polyps can be seen in familial adenomatous polyposis, they are not typically associated with gastric cancer in the absence of familial adenomatous polyposis. There is some evidence that selenium may be protective against gastric cancer. Whipple's disease is a rare infectious condition that causes digestive and joint issues; it is not typically associated with gastric cancer.

REFERENCE

Thrift AP, El-Serag HB. Burden of Gastric Cancer. *Clin Gastroenterol Hepatol.* 2020;18(3):534-542. doi:10.1016/j.cgh.2019.07.045

Question 28

A 65-year-old man from Ecuador undergoes upper

endoscopy for dyspepsia symptoms. Several small nonbleeding ulcers are noted in the antrum; biopsies reveal a chronic active gastritis with superficial band of lymphoplasmacytic cells without neutrophils.

Which of the following is true?

- A. These findings are likely due to a caustic ingestion
- B. Repeat endoscopy in 3 months is indicated
- C. Testing and treating for *Helicobacter pylori* may reduce gastric cancer risk
- D. Investigation for gastrinoma is indicated
- E. He should be referred to a surgeon

CORRECT ANSWER: C

RATIONALE

The histopathologic description is consistent with *Helicobacter pylori* (*H pylori*) infection. Testing and treating for *H pylori* may reduce gastric cancer risk. Pathology description is not consistent with caustic ingestion. Repeat endoscopy and/or surgery are not typically recommended to confirm ulcer healing in the absence of concern for associated gastric cancer.

REFERENCES

Leung WK, Wong IOL, Cheung KS, et al. Effects of *Helicobacter pylori* Treatment on Incidence of Gastric Cancer in Older Individuals. *Gastroenterology.* 2018;155(1):67-75. doi:10.1053/j.gastro.2018.03.028

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Question 29

A 52-year-old woman undergoes bidirectional endoscopy for iron deficiency anemia. A shallow gastric

ulcer is noted; biopsies are consistent with a gastric mucosa-associated lymphoid tissue lymphoma.

Which of the following statements is true?

- A. This tumor is rarely associated with *Helicobacter pylori*
- B. She should be referred to surgery for resection
- C. The tumor contains the 11:18 translocation
- D. The tumor has a poor prognosis compared with other gastric tumors
- E. High-dose proton pump therapy may cause regression

CORRECT ANSWER: C

RATIONALE

Gastric mucosa-associated lymphoid tissue lymphomas are characterized by the 11:18 translocation. They are often associated with *Helicobacter pylori* (*H pylori*) infection and may regress with treatment of *H pylori*. Surgery is no longer recommended as a first-line therapy. Although high-dose PPI may be part of *H pylori* treatment, it will not cause the tumor to regress in the absence of *H pylori* therapy.

REFERENCES

Parsonnet J, Hansen S, Rodriguez L, et al. Helicobacter pylori infection and gastric lymphoma. *N Engl J Med*. 1994;330(18):1267-1271. doi:10.1056/NEJM199405053301803

Steinbach G, Ford R, Globler G, et al. Antibiotic treatment of gastric lymphoma of mucosa-associated lymphoid tissue. An uncontrolled trial. *Ann Intern Med*. 1999;131(2):88-95. doi:10.7326/0003-4819-131-2-199907200-00003

Question 30

A 23-year-old woman with a pathogenic germline *MSH2* variant presents to your office. Her father died of gastric cancer at 57 years of age. She asks about her gastric cancer risk.

How should you counsel her?

- A. Aspirin 600 mg daily has been shown to reduce gastric cancer risk
- B. She should take a daily proton pump inhibitor
- C. She should undergo upper endoscopy
- D. No increased gastric cancer risk has been noted with *MSH2*
- E. Check for *Helicobacter pylori* (*H pylori*) and treat if positive

CORRECT ANSWER: E

RATIONALE

Patients with Lynch syndrome, in particular those with *MSH2* variants, may be at increased risk of gastric cancer. *H pylori* testing may be considered, and treatment of *H pylori* is recommended if detected. Patients with Lynch syndrome may consider upper endoscopy starting around the age of 40, and surveillance every 3-5 years, particularly in the setting of risk factors such as *MLH1/MSH2* pathogenic variants, male sex, residing in or immigrating from high-risk area, gastric intestinal metaplasia, chronic autoimmune gastritis, and a first-degree relative with gastric cancer. Aspirin 600 mg daily has been shown to decreased colorectal, but not gastric, cancer risk in patients with Lynch syndrome.

REFERENCES

Burn J, Sheth H, Elliott F, et al. Cancer prevention with aspirin in hereditary colorectal cancer (Lynch syndrome), 10-year follow-up and registry-based 20-year data in the CAPP2 study: a double-blind, randomised, placebo-controlled trial. *Lancet*. 2020;395(10240):1855-1863. doi:10.1016/S0140-6736(20)30366-4

Vasen HF, Blanco I, Aktan-Collan K, et al. Revised guidelines for the clinical management of Lynch syndrome (HNPCC): recommendations by a group of European experts. *Gut*. 2013;62(6):812-823. doi:10.1136/gutjnl-2012-304356

Weiss JM, Gupta S, Burke CA, et al. NCCN

Guidelines® Insights: Genetic/Familial High-Risk Assessment: Colorectal, Version 1.2021. *J Natl Compr Canc Netw*. 2021;19(10):1122-1132. Published 2021 Oct 15. doi:10.1164/jnccn.2021.0048

Question 31

A 50-year-old healthy man presents to your office. His partner was just diagnosed with gastric cancer, and he is concerned about his risk. Which of the following are true?

- A. Gastric cancer affects women more than men
- B. The incidence of proximal gastric cancer is decreasing
- C. Routine screening for gastric cancer is not warranted
- D. There is no difference in gastric cancer incidence between Black and White patients
- E. There is a lower incidence of gastric cancer in Hispanic patients compared with White patients

CORRECT ANSWER: C

RATIONALE

Gastric adenocarcinoma is the third leading cause of cancer death worldwide. Screening of the U.S. population is not warranted, except in certain high-risk situations. Risk increases with age, and men are at higher risk than women. Certain populations, such as Asian, Black, and Hispanic patients are at increased risk compared with White patients.

REFERENCES

Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [published correction appears in *CA Cancer J Clin*. 2020 Jul;70(4):313]. *CA Cancer J Clin*. 2018;68(6):394-424. doi:10.3322/caac.21492

Thrift AP, El-Serag HB. Burden of Gastric Cancer. *Clin Gastroenterol Hepatol*. 2020;18(3):534-542. doi:10.1016/j.cgh.2019.07.045

Question 32

A 60-year-old woman undergoes upper endoscopy for dyspepsia. Random biopsies of the stomach reveal 1 foci of complete gastric intestinal metaplasia (GIM) in the antrum. How should you counsel her regarding further management?

- A. She should be tested for *Helicobacter pylori* (*H pylori*), eradicate if found
- B. She should undergo short-interval repeat endoscopy with mapping biopsies
- C. Endoscopic surveillance has been demonstrated to improve survival
- D. There is no association between GIM and malignancy
- E. Risk of cancer is greater with complete GIM compared with incomplete GIM

CORRECT ANSWER: A

RATIONALE

GIM is believed to be the histologic precursor before development of dysplasia. The AGA recommends testing and treating for *H pylori* (compared with a strategy of no testing or treating) in patients with GIM. Routine surveillance is not typically recommended in the absence of other risk factors, such as incomplete versus complete GIM, extensive versus limited GIM, family history of gastric cancer, and risk based on country of origin, or racial/ethnic risk. Certain individuals with risk factors who place high value on the unknown possible benefits/low value on risk of surveillance may consider surveillance at uncertain intervals.

REFERENCE

Gupta S, Li D, El Serag HB, et al. AGA Clinical Practice Guidelines on Management of Gastric Intestinal Metaplasia. *Gastroenterology*. 2020;158(3):693-702. doi:10.1053/j.gastro.2019.12.003

Question 33

A 40-year-old woman presents to your office to discuss cancer risks. Her sister was just diagnosed

with stomach cancer at age 39, and her mother and grandmother had lobular breast cancer in their late 40s.

How should you counsel her?

- A. She should undergo genetic testing for *BRCA1*, *BRCA2*, and *PALB2*
- B. This syndrome is associated with nail dystrophy
- C. A *CTNNA1* variant may be identified in her family
- D. Her sister's gastric cancer likely arose from mesenchymal cells
- E. Family members may exhibit hyperpigmentation of the buccal mucosa

CORRECT ANSWER: C

RATIONALE

This family meets criteria for hereditary diffuse gastric cancer (HDGC). Although *CDH1* is the gene most commonly associated with HDGC, other genes such as *CTNNA1* are also associated with HDGC. Cronkhite-Canada syndrome is a rare acquired (nonhereditary) disease characterized by intestinal polyposis leading to malabsorption, hair loss, and nail dystrophy. Gastrointestinal stromal tumors are the most common mesenchymal tumor of the gastrointestinal tract. HDGC tumors are typically a diffuse type, often characterized by the presence of signet ring cells. Hyperpigmentation of the buccal mucosa is noted in Peutz-Jeghers syndrome, not HDGC.

REFERENCE

Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol*. 2015;110(2):223-263. doi:10.1038/ajg.2014.435

Question 34

A 25-year-old woman with familial adenomatous polyposis (FAP) presents to your office. She

underwent colectomy last year due to the presence of advanced adenomas and recovery has been uneventful. You perform an upper endoscopy, including a side-viewing examination, which reveals many fundic gland polyps in the stomach and 4 duodenal polyps less than 3 mm in size. The ampulla was normal. Biopsies of the duodenal polyps reveal tubular adenoma (mild dysplasia).

What is the next best step in management?

- A. Referral to a surgeon for gastrectomy
- B. Referral to a surgeon for pancreaticoduodenectomy
- C. Endoscopic upper gastrointestinal surveillance in 2-3 years
- D. Endoscopic upper gastrointestinal surveillance in 6-12 months
- E. Chemoprevention for progression of duodenal adenomas

CORRECT ANSWER: C

RATIONALE

The Spigelman stage have traditionally been used to determine surveillance strategies in FAP. This patient has Spigelman stage I, where surveillance is recommended in 2 to 3 years. Spigelman stage increases with polyp burden (both number and size) as well as more advanced histology (tubulovillous or villous) and dysplasia. For those with stages III/IV, surveillance in 3 to 6 months may be considered along with referral to surgery to discuss resection of duodenal pathology. Chemoprevention is not typically recommended at low Spigelman stage; studies are ongoing. Although recent research has raised concerns for increasing gastric cancer risk in FAP, fundic gland polyps are typically benign in this setting and gastrectomy is not indicated.

REFERENCE

Gupta S, Provenzale D, Llor X, et al. NCCN Guidelines Insights: Genetic/Familial High-Risk Assessment: Colorectal, Version 2.2019. *J Natl Compr Canc Netw*. 2019;17(9):1032-1041. doi:10.6004/jnccn.2019.0044

Question 35

A 42-year-old man with celiac disease presents to your office. He is particularly concerned about his risk for small bowel cancers.

Which of the following is true about small bowel tumors associated with celiac disease?

- A. These tumors arise from a B-cell clone
- B. These cancers typically present in younger individuals
- C. Tumors typically express CD3 and CD7
- D. They are most often located in the terminal ileum
- E. Patients are often asymptomatic

CORRECT ANSWER: C

RATIONALE

Enteropathy-associated T-cell lymphomas are rare small bowel tumors, often associated with celiac disease, and they are more often found in older individuals. They typically express common T-cell markers, such as CD3 and CD7. The most common site is in the jejunum. Patients often present with abdominal pain, B symptoms, symptoms of celiac disease/deterioration of celiac disease despite adherence to gluten-free diet, and/or intestinal obstruction, perforation or bleeding.

REFERENCE

Cellier C, Delabesse E, Helmer C, et al. Refractory sprue, coeliac disease, and enteropathy-associated T-cell lymphoma. French Coeliac Disease Study Group. *Lancet*. 2000;356(9225):203-208. doi:10.1016/S0140-6736(00)02481-8

Question 36

A 72-year-old man presents with abdominal pain, diarrhea, and weight loss. Endoscopic evaluation reveals a 1.5-cm ulcerated submucosal nodule in the terminal ileum. Biopsies demonstrate round nuclei with stippled chromatin; stains are positive for synaptophysin and neuron-specific enolase.

Which of the following are true about this finding?

- A. Metastatic disease is uncommon due to small size
- B. Incidence of these tumors is decreasing
- C. Vasoactive intestinal peptide secretion caused the diarrhea
- D. This arises from enterochromaffin cells in the crypts of Lieberkuhn
- E. Concomitant evaluation for celiac disease is warranted

CORRECT ANSWER: D

RATIONALE

This is likely a small bowel carcinoid tumor, which is a rare neuroendocrine tumor that arises from enterochromaffin cells located in the crypts of Lieberkuhn. Metastatic disease is common, even when the tumor is small (<2 cm). Incidence of these tumors is increasing, and neuroendocrine tumors have surpassed small bowel adenocarcinoma as the most common small bowel tumor. Vasoactive intestinal peptide secretion can be seen in a VIPoma, which is a rare pancreatic neuroendocrine tumor. Enteropathy-associated T-cell lymphomas, not neuroendocrine tumors, are associated with celiac disease.

REFERENCE

Strosberg J. Neuroendocrine tumours of the small intestine. *Best Pract Res Clin Gastroenterol*. 2012;26(6):755-773. doi:10.1016/j.bpg.2012.12.002

Question 37

A 68-year-old woman is incidentally found to have a sub-centimeter neuroendocrine tumor of the terminal ileum on screening colonoscopy. She is asymptomatic.

Which of the following is true?

- A. Small bowel adenocarcinoma is more common than small bowel neuroendocrine tumors
- B. These tumors are commonly metastatic on presentation

- C. She should be treated with octreotide
- D. Genetic testing is warranted
- E. 5-year survival is <10%

CORRECT ANSWER: B

RATIONALE

Small bowel neuroendocrine tumors are often metastatic at time of presentation, even when they are small (<2 cm). Neuroendocrine tumors have surpassed adenocarcinoma as the leading cause of small bowel tumors, possibly due to increased small bowel evaluation with capsule endoscopy and deep enteroscopy. Octreotide can be used to manage symptoms of carcinoid syndrome; she is asymptomatic. Genetic testing is not warranted for these tumors in the absence of other factors. Survival for small bowel neuroendocrine tumors is better than for adenocarcinomas; even for metastatic disease; 5-year survival is approximately 40%.

REFERENCES

Kim MK, Warner RR, Roayaie S, et al. Revised staging classification improves outcome prediction for small intestinal neuroendocrine tumors. *J Clin Oncol*. 2013;31(30):3776-3781. doi:10.1200/JCO.2013.51.1477

Rorstad O. Prognostic indicators for carcinoid neuroendocrine tumors of the gastrointestinal tract. *J Surg Oncol*. 2005;89(3):151-160. doi:10.1002/jso.20179

Question 38

A 46-year-old man with pan-ulcerative colitis presents with 3 weeks of jaundice. Complete blood count, platelets, and albumin are normal.

Additional laboratory results are below.

Magnetic resonance cholangiogram demonstrates a dominant extrahepatic stricture with proximal dilation.

What is the next best step in management?

- A. Start ursodeoxycholic acid
- B. Refer for liver transplant evaluation
- C. Refer for endoscopic retrograde cholangiopancreatography
- D. Prescribe antibiotics
- E. Refer for surgical resection

CORRECT ANSWER: C

RATIONALE

This patient has ulcerative colitis and now presents with primary sclerosing cholangitis (PSC) and a dominant stricture, placing him at increased risk for cholangiocarcinoma. Lifetime risk of cholangiocarcinoma in patients with PSC is 10% to 15%, and this risk increases with the presence of a dominant stricture. Bile duct tissue sampling is required to evaluate for cholangiocarcinoma. Ursodeoxycholic acid does not have benefit in PSC. The patient has normal hepatic synthetic function; therefore, liver transplant evaluation is not required at this time. Clinical presentation is not consistent with bacterial cholangitis; therefore, antibiotics is not the correct answer. Surgical resection of dominant stricture is no longer the preferred technique.

REFERENCE

Yachimski P, Pratt DS. Cholangiocarcinoma: natural history, treatment, and strategies for

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	525	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	87	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	90	10-40
Bilirubin, serum		
Total, mg/dL	8.5	0.3-1.0
Direct, mg/dL	5.2	0.1-0.3

surveillance in high-risk patients. *J Clin Gastroenterol.* 2008;42(2):178-190. doi:10.1097/MCG.0b013e31806daf89

Question 39

A 63-year-old man presents with abdominal fullness and early satiety. Computed tomography demonstrates a mass in the gallbladder fossa, and biopsy confirms adenocarcinoma.

Which of the following is a risk factor for gallbladder cancer?

- A. *Clonorchis sinensis* infection
- B. Male sex
- C. Calcification of the gallbladder wall
- D. *Opisthorchis viverrini* infection
- E. Primary sclerosing cholangitis

CORRECT ANSWER: C

RATIONALE

Infection with liver flukes, such as *Opisthorchis viverrini* and *Clonorchis sinensis*, and primary sclerosing cholangitis are risk factors for cholangiocarcinoma, not gallbladder carcinoma. Gallbladder cancers have a female preponderance, and they are more common in individuals of Mexican, Chilean, Bolivian, Native American, and Japanese descent. Other risk factors include gallstones, gallbladder polyps (particularly >1 cm), and calcification of the gallbladder wall (porcelain gallbladder).

REFERENCE

Rawla P, Sunkara T, Thandra KC, Barsouk A. Epidemiology of gallbladder cancer. *Clin Exp Hepatol.* 2019;5(2):93-102. doi:10.5114/ceh.2019.85166

Question 40

A 72-year-old man presents with jaundice. He worked in construction and drinks 2 beers daily. His brother and father had pancreatitis. Imaging reveals proximal biliary dilation and a mass at the bifurcation. Tissue sampling confirms cholangiocarcinoma.

Which of the following is a risk factor for this patient's cancer?

- A. Hereditary pancreatitis
- B. Previous iodinated contrast dye
- C. Primary biliary cholangitis
- D. Gallbladder polyps
- E. Asbestos exposure

CORRECT ANSWER: E

RATIONALE

Risk factors for cholangiocarcinoma include asbestos exposure, tobacco use, choledochal cysts, and Caroli disease (multiple cystic dilations of the biliary tree). Exposure to thorium dioxide ("Thorotrast"), which is a previously used radiologic contrast agent, is associated with increased risk of cholangiocarcinoma; iodinated contrast dye is not. Hereditary pancreatitis predisposes to pancreatic cancer, not cholangiocarcinoma. Gallbladder polyps are associated with gallbladder cancer.

REFERENCE

Bergquist A, von Seth E. Epidemiology of cholangiocarcinoma. *Best Pract Res Clin Gastroenterol.* 2015;29(2):221-232. doi:10.1016/j.bpg.2015.02.003

Question 41

A 32-year-old man with familial adenomatous polyposis (FAP) presents for management of an ampullary adenoma. Upper endoscopy and endoscopic ultrasound demonstrate a 1.3-cm adenoma without intraductal growth; biopsies reveal low-grade dysplasia. More than 20 duodenal polyps are noted, several of which are larger than 1 cm; tubulovillous histology is noted on 1 polyp.

Which of the following do you recommend for management of the adenoma?

- A. Endoscopic resection
- B. Endoscopic surveillance
- C. Surgical referral

- D. Chemoprevention
- E. No further management

CORRECT ANSWER: C

RATIONALE

Although the ampullary adenoma may be amenable to endoscopic resection or further surveillance, neither of these approaches are recommended in the setting of Spigelman stage IV duodenal polyposis in FAP. Ongoing studies are investigating the role of chemoprevention in FAP.

REFERENCE

ASGE Standards of Practice Committee, Chathadi KV, Khashab MA, et al. The role of endoscopy in ampullary and duodenal adenomas. *Gastrointest Endosc.* 2015;82(5):773-781. doi:10.1016/j.gie.2015.06.027

Question 42

A 52-year-old woman comes to your office to discuss her risk of pancreatic cancer. Her mother died of pancreatic cancer at 68, and her sister was just diagnosed with breast cancer at age 49. Her sister reports a “positive” genetic testing result.

Which of the following genes are associated with increased pancreatic cancer risk?

- A. *SMAD4*
- B. *CDH1*
- C. *CHEK2*
- D. *ATM*
- E. *MUTYH*

CORRECT ANSWER: D

RATIONALE

Pathogenic variants in *SMAD4* are associated with juvenile polyposis syndrome. These patients develop multiple juvenile polyposis throughout the gastrointestinal tract. They have increased risk of colorectal and possibly stomach cancer and may develop hereditary hemorrhagic telangiectasia.

Pathogenic *CDH1* mutations are associated with hereditary diffuse gastric cancer and lobular breast cancer, whereas *CHEK2* is associated with breast cancer and a modest increased risk of colorectal cancer. Pathogenic variants in *ATM*, *BRCA2*, *STK11* (Peutz-Jeghers syndrome), *PALB2*, and the mismatch repair genes (Lynch syndrome) have been associated with increased risk of pancreatic cancer. Monoallelic germline mutations in *ATM* are also associated with increased risk of breast cancer. Monoallelic mutations in *MUTYH* are thought to confer a modest increased risk in colorectal cancer, whereas biallelic *MUTYH* mutations cause a colonic polyposis syndrome known as *MUTYH*-associated polyposis (MAP).

REFERENCES

Goggins M, Overbeek KA, Brand R, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. *Gut.* 2020;69(1):7-17. doi:10.1136/gutjnl-2019-319352

Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol.* 2015;110(2):223-263. doi:10.1038/ajg.2014.435

Question 43

A 65-year-old man is hospitalized due to epigastric pain and a 25-pound weight loss. Abdominal imaging demonstrates dilated biliary and pancreatic ducts, a mass in the head of the pancreas involving the splenic artery, and a 2.3-cm mass in the left lobe of the liver. Biopsy of the liver lesion reveals poorly differentiated adenocarcinoma.

Which of the following do you recommend?

- A. Choledochojejunostomy
- B. Pancreaticoduodenectomy with left hepatic lobectomy
- C. Gastrostomy tube placement

- D. Endoscopic retrograde cholangiopancreatography with stent placement
- E. Percutaneous biliary drainage

CORRECT ANSWER: D

RATIONALE

Endoscopic retrograde cholangiopancreatography with stent placement is recommended for this patient with metastatic pancreatic adenocarcinoma. Percutaneous drainage may be considered if endoscopic decompression fails. Surgical resection of the tumor and/or metastatic liver lesion is not recommended at this time.

REFERENCE

Tempero MA, Malafa MP, Al-Hawary M, et al. Pancreatic Adenocarcinoma, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2021;19(4):439-457. Published 2021 Apr 1. doi:10.6004/jnccn.2021.0017

Question 44

A 70-year-old woman with diabetes diagnosed 1 year ago presents to the hospital with confusion, diarrhea, and a 15-pound weight loss. Family has noted an erythematous, crusted rash on her legs.

Which of the following is likely to establish the diagnosis?

- A. Fasting plasma vasoactive intestinal peptide
- B. Fasting serum glucagon
- C. Fasting serum insulin and glucose
- D. Fasting serum gastrin
- E. Fasting chromogranin

CORRECT ANSWER B

RATIONALE

This patient has a glucagonoma, characterized by classic rash known as necrolytic migratory erythema and glucose intolerance/diabetes. Elevated vasoactive intestinal peptide levels are consistent

with VIPoma, which causes WDHA (watery diarrhea, dehydration, hypokalemia, achlorhydria). Insulinomas are characterized by hypoglycemia and elevated insulin levels. Elevated gastrin levels are seen in a gastrinoma, or Zollinger-Ellison syndrome. Chromogranin levels are nonspecific markers of neuroendocrine tumors.

REFERENCE

Lee DW, Kim MK, Kim HG. Diagnosis of Pancreatic Neuroendocrine Tumors. *Clin Endosc*. 2017;50(6):537-545. doi:10.5946/ce.2017.131

Question 45

A 63-year-old woman with hypothyroidism is hospitalized due to epigastric pain and jaundice. Abdominal computed tomography demonstrates a 1.3-cm mass in the head of the pancreas without vascular invasion. The pancreatic duct and common bile ducts are dilated. Endoscopic ultrasound with fine needle aspiration demonstrates atypical cytology. Endoscopic retrograde cholangiopancreatography was performed, and plastic stents were placed.

What is the next best step for this patient?

- A. Check immunoglobulin G4 (IgG4) levels
- B. Trial of corticosteroids
- C. Repeat endoscopic ultrasound with fine needle aspiration
- D. Surgical referral
- E. Endoscopic retrograde cholangiopancreatography with bile duct sampling

CORRECT ANSWER: D

RATIONALE

This patient likely has pancreatic adenocarcinoma and should be referred for surgical evaluation. Pancreatic imaging is not consistent with autoimmune pancreatitis; therefore, IgG4 levels and corticosteroids are incorrect. With a high index of suspicion of pancreatic adenocarcinoma, patient should be referred for surgical evaluation.

REFERENCE

Tempero MA, Malafa MP, Al-Hawary M, et al. Pancreatic Adenocarcinoma, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2021;19(4):439-457. Published 2021 Apr 1. doi:10.6004/jnccn.2021.0017

Question 46

A 59-year-old man is admitted to the hospital with 3 weeks of jaundice and mid-abdominal discomfort. Computed tomography demonstrates a 2.4-cm cyst in the head of the pancreas. Endoscopic ultrasound demonstrates cyst fluid carcinoembryonic antigen level of 327 ng/mL and cytology is acellular. Endoscopic retrograde cholangiopancreatography is also performed and a stent is placed for biliary decompression.

What is the next best step in management?

- A. Computed tomography in 3-6 months
- B. Immunoglobulin G4 (IgG4) levels and trial of steroids
- C. Repeat endoscopic ultrasound-fine needle aspiration of the cyst
- D. Surgical referral
- E. Magnetic resonance imaging with magnetic resonance cholangiopancreatography

CORRECT ANSWER: D

RATIONALE

Jaundice in the setting of a pancreatic cystic lesion such as intraductal papillary mucinous neoplasm is a high-risk feature that warrants surgical consultation. Imaging is not consistent with autoimmune pancreatitis and there is a high index of suspicion for cancer; therefore, IgG4 levels and a trial of corticosteroids is not appropriate. Although additional tests may be considered, the next best step is referral for surgical consultation.

REFERENCE

Tanaka M, Fernández-Del Castillo C, Kamisawa T, et al. Revisions of international consensus Fu-

kuoka guidelines for the management of IPMN of the pancreas. *Pancreatology*. 2017;17(5):738-753. doi:10.1016/j.pan.2017.07.007

Question 47

A 62-year-old woman presents for endoscopic ultrasound after a pancreatic lesion was noted on imaging for a renal cyst.

Which of the following features is most specific for the presence of an intraductal papillary mucinous neoplasm (IPMN)?

- A. Honeycombed appearance
- B. Central scar
- C. Mucin extruding from ampulla
- D. Female predominance
- E. Cyst fluid carcinoembryonic antigen <192 ng/mL

CORRECT ANSWER: C

RATIONALE

Mucin extruding from the ampulla of Vater is most consistent with an IPMN. Honeycombed appearance and central scar are found in serous cystadenomas. Female preponderance is noted in mucinous cystic neoplasms; no sex differences are noted in IPMNs. Cyst fluid carcinoembryonic antigen levels higher than 192 ng/mL are consistent with a mucinous lesion, such as IPMN or mucinous cystic neoplasms.

REFERENCE

Turner BG, Brugge WR. Diagnostic and therapeutic endoscopic approaches to intraductal papillary mucinous neoplasm. *World J Gastrointest Surg*. 2010;2(10):337-341. Doi:10.4240/wjgs.v2.i10.337

Question 48

A 56-year-old woman is referred to you for evaluation of a 2.5-cm pancreatic tail lesion with large cystic components found on abdominal computed tomography for diverticulitis. Endoscopic ultra-

sound demonstrated cyst fluid carcinoembryonic antigen (CEA) level of 526 ng/mL.

Which of the following is the most likely diagnosis?

- A. Intraductal papillary mucinous neoplasm
- B. Adenocarcinoma
- C. Serous cystadenoma
- D. Mucinous cystic neoplasm
- E. Pseudocyst

CORRECT ANSWER: D

RATIONALE

Mucinous cystic neoplasms (MCNs) are typically oligocystic lesions with large cystic components in the body or tail of the pancreas. They are almost exclusively noted in women. CEA levels higher than 192 ng/mL are suggestive of mucinous lesions, such as intraductal papillary mucinous neoplasms or MCNs. However, the oligocystic description of the cyst on cross-sectional imaging is more suggestive of a MCN than intraductal papillary mucinous neoplasms. Aspiration from serous cystadenoma or pseudocyst is not likely to yield cyst fluid CEA levels higher than 192 ng/mL.

REFERENCES

Elta GH, Enestvedt BK, Sauer BG, Lennon AM. ACG Clinical Guideline: Diagnosis and Management of Pancreatic Cysts. *Am J Gastroenterol*. 2018;113(4):464-479. doi:10.1038/ajg.2018.14

Lennon AM, Ahuja N, Wolfgang CL. AGA Guidelines for the Management of Pancreatic Cysts. *Gastroenterology*. 2015;149(3):825. doi:10.1053/j.gastro.2015.05.062

Scheiman JM, Hwang JH, Moayyedi P. American gastroenterological association technical review on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. *Gastroenterology*. 2015;148(4):824-48.e22. doi:10.1053/j.gastro.2015.01.014

Question 49

A 61-year-old woman is referred to you for follow-up of diverticulitis. A computed tomography in the emergency department revealed diverticulitis and a 15-mm multicystic structure in the body of the pancreas with a central scar. She had a colonoscopy 6 months ago with sigmoid diverticulosis. Overall, she feels well and has no abdominal discomfort.

What do you recommend for evaluation of the pancreatic lesion?

- A. Magnetic resonance imaging
- B. Endoscopic ultrasound
- C. Computed tomography with pancreas protocol
- D. Surgical resection
- E. No further evaluation

CORRECT ANSWER: E

RATIONALE

This patient has a serous cystadenoma, for which no further evaluation is required. Serous cystadenomas may have a central fibrosis scar or calcification and are typically multicystic, lobulated structures sometimes described as “a bunch of grapes.” If the diagnosis is uncertain, further imaging may be considered. However, this lesion has classic features of a serous cystadenoma and no imaging is required. These lesions are benign and the patient is asymptomatic; therefore, surgical resection is not indicated.

REFERENCE

Elta GH, Enestvedt BK, Sauer BG, Lennon AM. ACG Clinical Guideline: Diagnosis and Management of Pancreatic Cysts. *Am J Gastroenterol*. 2018;113(4):464-479. doi:10.1038/ajg.2018.14

Question 50

A 52-year-old healthy woman presents to your office with 1 month of abdominal discomfort and 5-pound weight loss. Routine laboratory tests are normal. Abdominal computed tomography shows

a 2-cm mass in the head of the pancreas with a solitary liver lesion consistent with metastasis. Biopsy shows small cells with finely granular cytoplasm and a “salt and pepper” appearance of chromatin.

Which of the following is the best management option?

- A. Stereotactic radiation
- B. Palliative chemotherapy
- C. Surgical resection
- D. Liver transplantation
- E. Biliary stent placement

CORRECT ANSWER: C

RATIONALE

This patient has a pancreatic neuroendocrine tumor, which may be managed with surgical resection and debulking. Management of neuroendocrine tumors differs from that of pancreatic adenocarcinoma; if this were an adenocarcinoma, palliative chemotherapy would be an appropriate management choice.

REFERENCE

Pavel M, Baudin E, Couvelard A, et al. ENETS Consensus Guidelines for the management of patients with liver and other distant metastases from neuroendocrine neoplasms of foregut, midgut, hindgut, and unknown primary. *Neuroendocrinology*. 2012;95(2):157-176. doi:10.1159/000335597

CHAPTER 15

Nutrition, obesity and eating disorders

Octavia Pickett-Blakely, MD and Justin Crocker, MD

Question 1

You are asked to evaluate a 42-year-old woman with hypertension and type 2 diabetes who is experiencing nausea and fatigue 2 weeks after undergoing intragastric balloon placement for class 2 obesity (body mass index 35–40 kg/m²). She reports limited oral intake due to nausea. On examination, she is afebrile, heart rate is 87 bpm, blood pressure is 116/76 mmHg, weight is 90 kg (down from 94 kg), and body mass index is 32 kg/m². Abdominal examination reveals mild tenderness in the epigastrium, but no rebound or guarding. Medications include calcium carbonate as needed for dyspepsia, ondansetron, amlodipine, and glyburide.

Which of the following medications is recommended to reduce complications after intragastric balloon placement?

- A. Oral iron supplementation
- B. Proton pump inhibitor
- C. Analgesics
- D. Osmotic laxatives
- E. Vitamin D supplementation

CORRECT ANSWER: B

RATIONALE

The recently published AGA Clinical Practice Guidelines strongly recommend proton pump inhibitor prophylaxis in patients undergoing

intragastric balloon placement based on moderate quality of evidence indicating a lower risk of nonprocedure-related adverse events.

REFERENCE

Muniraj T, Day LW, Teigen LM, et al. AGA Clinical Practice Guidelines on Intragastric Balloons in the Management of Obesity. *Gastroenterology*. 2021;160(5):1799–1808. doi:10.1053/j.gastro.2021.03.003

Question 2

A 51-year-old man with obesity, hypertension, dyslipidemia, gastroesophageal reflux, and chronic constipation seeks evaluation for worsening constipation symptoms. He reports 1 Bristol stool scale type 2 bowel movement weekly with straining, which is decreased from his baseline of every other day. He reports no dietary changes. He denies abdominal distension or vomiting. On examination, he is afebrile, heart rate is 75 bpm, blood pressure is 146/88 mmHg, and body mass index is 34 kg/m². Abdominal examination reveals a soft, nontender, nondistended abdomen. A colonoscopy 3 months ago was normal, with no polyps. Medications include candesartan, omeprazole, polyethylene glycol, and liraglutide.

Which of the following is the most likely culprit for his worsening constipation?

- A. Inadequate hydration
- B. Pelvic dyssynergia
- C. Low dietary fiber
- D. Liraglutide
- E. Omeprazole

CORRECT ANSWER: D

RATIONALE

The etiology of constipation can be multifactorial in such a patient. However, inadequate hydration is unlikely to be the sole etiology of his constipation. Pelvic dyssynergia is unlikely in a 51-year-old man. Although low dietary fiber is a possible explanation, he recently had worsening of constipation in the absence of dietary changes. Due to the mediated effects of liraglutide from glucagon-like peptide-1, early satiety, nausea, vomiting, and constipation are common adverse effects of the drug. Constipation is not a common adverse effect of omeprazole.

REFERENCE

Tak YJ, Lee SY. Long-Term Efficacy and Safety of Anti-Obesity Treatment: Where Do We Stand?. *Curr Obes Rep.* 2021;10(1):14-30. doi:10.1007/s13679-020-00422-w

Question 3

Which of the following is recommended to augment and maintain weight loss after intragastric balloon placement according to American Gastroenterological Association (AGA) guidelines?

- A. Glucagon-like peptide-1 analog
- B. Low- to moderate-intensity lifestyle modifications
- C. Bariatric surgery referral
- D. Moderate- to high-intensity lifestyle modifications
- E. Sympathomimetic appetite suppressant

CORRECT ANSWER: D

RATIONALE

The AGA clinical practice guidelines on intra-

gastric balloons in the management of obesity recommend moderate- to high-intensity lifestyle modification to augment and maintain weight loss in those undergoing intragastric balloons. There is limited data on concomitant obesity pharmacotherapy in patients undergoing intragastric balloon therapy; therefore, at this time, it is not recommended in the clinical practice guidelines. Patients who have recently undergone intragastric therapy alone can be considered for bariatric surgery referral if weight loss is not achieved with balloon therapy.

REFERENCE

Muniraj T, Day LW, Teigen LM, et al. AGA Clinical Practice Guidelines on Intragastric Balloons in the Management of Obesity. *Gastroenterology.* 2021;160(5):1799-1808. doi:10.1053/j.gastro.2021.03.003

Question 4

A 33-year-old woman comes in for evaluation of change in bowel habits. She reports postprandial urgent bowel movements with flatus and oil droplets in her stool. She reports that she is trying to lose weight in preparation for her sister's wedding, and she recently started a high-intensity exercise program and weight loss medication.

Which of the following medications is the most likely culprit for her symptoms?

- A. Liraglutide
- B. Phentermine
- C. Semaglutide
- D. Orlistat
- E. Bupropion/naltrexone

CORRECT ANSWER: D

RATIONALE

Orlistat is approved by the US Food and Drug Administration for obesity treatment. The mechanism of action is lipase inhibition, which can lead to fat maldigestion and steatorrhea. This adverse

effect is proportionally linked to dietary fat, and this information can be used in counseling patients who are using this drug.

REFERENCE

Tak YJ, Lee SY. Long-Term Efficacy and Safety of Anti-Obesity Treatment: Where Do We Stand? *Curr Obes Rep.* 2021;10(1):14-30. doi:10.1007/s13679-020-00422-w

Question 5

A 42-year-old woman with a history of class 1 obesity, type 2 diabetes, dyslipidemia, and constipation presents to you inquiring about bariatric procedures for weight loss. She reports unsuccessful weight loss despite 6 months of lifestyle modification and exercise. In addition, she discloses that she discontinued liraglutide due to severe nausea and vomiting, and she does not want to try any other weight loss medications.

Which of the following options would you recommend for weight loss in this patient?

- A. Intra-gastric balloon placement
- B. Gastric aspiration therapy
- C. Laparoscopic sleeve gastrectomy
- D. Roux-en-Y gastric bypass

CORRECT ANSWER: A

RATIONALE

This patient should be considered for intra-gastric balloon therapy, which is approved by the US Food and Drug Administration as a weight loss option in class 1 obesity. Gastric aspiration therapy should be considered in patients with

class 2 or 3 obesity (body mass index >35 kg/m²), as it is effective for weight loss. Weight loss surgery should be considered in patients with class 2 obesity with a comorbid illness and class 3 obesity with or without comorbidities.

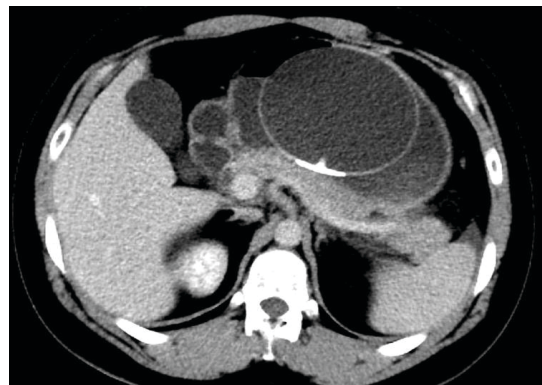
REFERENCE

Muniraj T, Day LW, Teigen LM, et al. AGA Clinical Practice Guidelines on Intra-gastric Balloons in the Management of Obesity. *Gastroenterology.* 2021;160(5):1799-1808. doi:10.1053/j.gastro.2021.03.003

Question 6

You are called to the emergency department to see a 25-year-old man presenting with acute abdominal pain. On history, he discloses that he recently returned from a trip abroad where he underwent a weight loss procedure. The pain is severe epigastric pain associated with nausea and vomiting. On examination, he is afebrile, heart rate is 105 bpm, blood pressure is 110/78 mmHg, oxygen saturation is 98% on room air. Results are shown below.

A computed tomography scan of the abdomen/pelvis is shown below.



ALSOHAIBANI FI ET AL. OBES SURG. 2019;29(5):1694-1696.

Laboratory Test	Result	Reference Range
Hemoglobin, blood, g/dL	12.5	14-18
Leukocyte (WBC) count, cells/ μ L	11,000	4000-11,000
Lipase, serum, U/L	1100	10-140
Platelet count, plt/ μ L	350,000	150,000-450,000

Which of the following is the best definitive therapy for this patient?

- A. Urgent surgical consultation
- B. Bowel rest, intravenous hydration, analgesia, antiemetics
- C. Broad spectrum antibiotics
- D. Endoscopy with foreign body removal
- E. Intravenous proton pump inhibitor

CORRECT ANSWER: D

RATIONALE

Gastric balloons have been used worldwide for many years as a weight loss therapy. Although there are several gastric balloons approved by the US Food and Drug Administration (FDA), gastric balloon placement is not covered by insurance in the US, and it is cost prohibitive for many patients, which results in some patients undergoing weight loss procedures abroad. This patient likely underwent endoscopic gastric balloon placement abroad. Nausea, vomiting, and abdominal pain are known adverse effects associated with gastric balloon placement that are most often managed with peri- and postprocedure hydration, antispasmodics, and antiemetics. However, there have been reports of acute pancreatitis (which is shown on the above image) associated with the gastric balloon for which there was an FDA warning published. Gastroenterologists should be aware of this complication of gastric balloon placement and the recommended treatment, which is balloon deflation and removal.

REFERENCES

Alsohaibani FI, Alkasab M, Abufarhaneh EH, et al. Acute Pancreatitis as a Complication of Intra-gastric Balloons: a Case Series. *Obes Surg*. 2019;29(5):1694-1696. doi:10.1007/s11695-019-03796-6

Yorke E, Switzer NJ, Reso A, et al. Intra-gastric Balloon for Management of Severe Obesity: a Systematic Review. *Obes Surg*. 2016;26(9):2248-2254. doi:10.1007/s11695-016-2307-9

Question 7

Which of the following obesity pharmacotherapies is contraindicated in a patient with primary intestinal lymphangiectasia?

- A. Phentermine
- B. Liraglutide
- C. Bupropion/naltrexone
- D. Orlistat

CORRECT ANSWER: D

RATIONALE

In choosing an appropriate pharmacotherapeutic option for obesity, one must consider comorbid medical conditions, concomitant medications, and cost. Phentermine is an adrenergic agonist that acts to suppress appetite. Liraglutide is a glucagon-like peptide-1 analogue that induces satiety, slows gastric emptying, and enhances pancreatic insulin production. Bupropion/naltrexone is a combined opioid receptor antagonist and dopamine and noradrenergic reuptake inhibitor that reduces hunger and cravings. Orlistat is a lipase inhibitor that inhibits fat digestion. Given its mechanism of action, orlistat is contraindicated in patients with malabsorptive syndromes such as primary intestinal lymphangiectasia, which increases the likelihood of developing fat-soluble vitamin deficiencies.

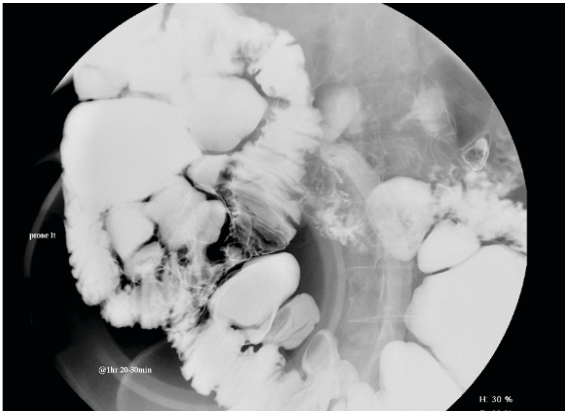
REFERENCE

Tak YJ, Lee SY. Long-Term Efficacy and Safety of Anti-Obesity Treatment: Where Do We Stand?. *Curr Obes Rep*. 2021;10(1):14-30. doi:10.1007/s13679-020-00422-w

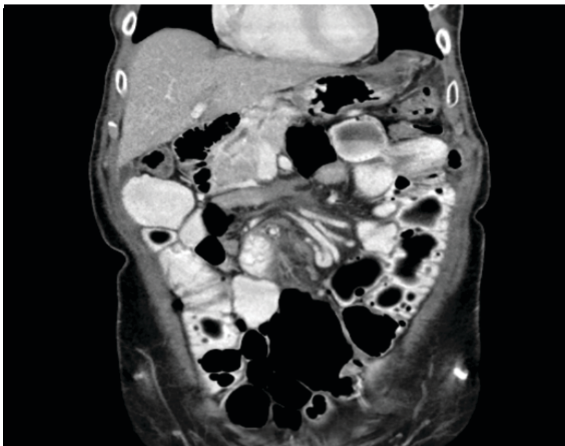
Question 8

A 75-year-old man presents for evaluation of nausea, abdominal bloating and distension, loose stools, and weight loss. On examination, he is afebrile with normal vital signs. Height is 1.7 m, weight is 82 kg, and body mass index is 28 kg/m². An initial workup including upper endoscopy with biopsies was essentially unremarkable.

Abdominal imaging is shown below.



Small bowel follow-through



Computed Tomography of abdomen/pelvis

What is the most likely micronutrient deficiency that you expect to find in this patient?

- A. Zinc
- B. Vitamin B12
- C. Iron
- D. Folate
- E. Vitamin C

CORRECT ANSWER: B

RATIONALE

This patient has small bowel diverticulosis and secondary, symptomatic small intestinal bacterial overgrowth (SIBO). Cyanocobalamin (vitamin B12) deficiency can occur in SIBO as a result of competitive uptake of vitamin B12. In SIBO, folate can be elevated due to bacterial synthesis.

Although zinc, iron, and vitamin C deficiency can occur in the context of weight loss, these micronutrients are not specifically deficient in SIBO.

REFERENCES

Quigley EMM, Murray JA, Pimentel M. AGA Clinical Practice Update on Small Intestinal Bacterial Overgrowth: Expert Review. *Gastroenterology*. 2020;159(4):1526-1532. doi:10.1053/j.gastro.2020.06.090

Rangan V, Lamont JT. Small Bowel Diverticulosis: Pathogenesis, Clinical Management, and New Concepts. *Curr Gastroenterol Rep*. 2020;22(1):4. Published 2020 Jan 15. doi:10.1007/s11894-019-0741-2

Question 9

A 23-year-old man with Crohn's ileocolitis who underwent an ileal resection for stricturing disease 8 months ago presents with left flank pain. He is found to have kidney stones, which he eventually passed and were found to be calcium oxalate stones.

Which of the following diets should you recommend?

- A. Low oxalate, low calcium
- B. Low oxalate, high calcium
- C. Low oxalate, low fat
- D. Low oxalate, high fat

CORRECT ANSWER: B

RATIONALE

Calcium oxalate stones can occur in patients with fat malabsorption, as in this case of a patient with ileal Crohn's disease with ileal resection. In the colon, malabsorbed fat binds preferentially to calcium, leaving oxalate unbound and free for colonic absorption and subsequent oxalate stone formation. Dietary recommendations focus on reduced dietary oxalate, increased calcium, and lower fat to enhance calcium binding to oxalate and excretion in the stool.

REFERENCE

Siener R. Nutrition and Kidney Stone Disease. *Nutrients*. 2021;13(6):1917. Published 2021 Jun 3. doi:10.3390/nu13061917

Question 10

A 52-year-old man presents for evaluation of diarrhea and weight loss after undergoing ileal resection for stricturing Crohn's disease. The pathology report indicates that the specimen contains "200 cm of small bowel" with transmural inflammation and noncaseating granulomas. He reports 5 to 10 nonbloody, watery bowel movements daily. A computed tomography enterography (CTE) shows no evidence of active disease.

Which of the following result(s) would you most likely obtain from his diarrhea evaluation?

- A. Elevated fecal calprotectin
- B. Low serum vitamins A, E, and D
- C. Elevated serum cyanocobalamin (vitamin B12)
- D. Low fecal elastase
- E. Osmotic gap of 125 mOsm/kg on stool electrolyte testing

CORRECT ANSWER: B

RATIONALE

This patient underwent ileal resection with 200 centimeters removed. The ileum is responsible for micronutrient and fluid absorption, particularly bile salts and vitamin B12. In patients with small volume ileal resection (<150 cm), vitamin B12 deficiency can occur as well as bile salt-mediated secretory diarrhea (cholorrheic diarrhea). In patients with larger volume ileal resection (> 150 cm), fat maldigestion and steatorrhea will occur, due to depletion of the overall bile acid pool. In addition to diarrhea, patients can have significant weight loss resulting from fat maldigestion and malabsorption; hence, one would also expect to see low serum fat-soluble vitamin levels. Given a normal CTE, the fecal calprotectin is

unlikely to be elevated. Serum vitamin B12 will be low due to decreased absorption in the ileum. Fecal elastase is low with pancreatic insufficiency, not fat malabsorption due to decreased small bowel absorptive capacity. The osmotic gap is calculated to differentiate between secretory and osmotic diarrhea; a gap greater than 100 denotes an osmotic diarrhea, and a gap less than 50 denotes a secretory diarrhea. This patient has a secretory diarrhea due to loss of absorptive capacity and would thus have a low osmotic gap.

REFERENCE

Carroll RE, Benedetti E, Schowalter JP, Buchman AL. Management and Complications of Short Bowel Syndrome: an Updated Review. *Curr Gastroenterol Rep*. 2016;18(7):40. Doi:10.1007/s11894-016-0511-3

Question 11

You see a 61-year-old woman with a remote history of Roux-en-Y gastric bypass for abdominal pain during a prolonged hospitalization for urosepsis. Her hospital course is complicated by deconditioning and decubitus ulcer. On review of systems, she also reports fatigue, dyspnea on exertion, and new changes in her memory. Her medications include oral ciprofloxacin, oxycodone, and zinc sulfate. On examination, vital signs are normal, and she has skin pallor, with normal cardiovascular and pulmonary examinations. There is mild epigastric tenderness to palpation with no rebound or guarding.

You perform an upper endoscopy, which reveals a small, nonbleeding anastomotic ulcer; her colonoscopy is normal. Two months later, the patient is seen by you in follow-up and reports some improvement in abdominal pain, but the fatigue, dyspnea on exertion, and memory problems persist.

Which of the following is the most likely micronutrient deficiency that would explain the patient's symptoms?

- A. Iron
- B. Magnesium
- C. Potassium
- D. Copper
- E. Folate

CORRECT ANSWER: D

RATIONALE

This patient has a history of a Roux-en-Y gastric bypass, which is a restrictive and malabsorptive weight loss procedure. Because of altered gastrointestinal tract anatomy, these patients are at risk for micronutrient deficiencies in the late postoperative period. Copper deficiency can occur in the setting of zinc supplementation due to competitive absorption of zinc in the proximal small bowel. Patients with copper deficiency can present with fatigue, weakness, cognitive impairment, gait changes, osteoporosis, and paresthesias.

REFERENCE

Via MA, Mechanick JI. Nutritional and Micronutrient Care of Bariatric Surgery Patients: Current Evidence Update. *Curr Obes Rep.* 2017;6(3):286-296. doi:10.1007/s13679-017-0271-x

Question 12

A 24-year-old man who had a traumatic bowel injury from a motor vehicle accident 7 months ago presents for evaluation of diarrhea. During the hospitalization, he underwent small bowel resection (80% of his small bowel including the ileum) and right hemicolectomy with end jejunostomy. He subsequently underwent jejunostomy take-

down with end-to-side enterocolonic anastomosis. Since his operation, he reports up to 20 nonbloody liquid bowel movements daily. He has had weekly emergency department visits for diarrhea, dehydration, and muscle cramps, which are treated with intravenous fluids and electrolyte supplementation.

He takes loperamide, famotidine, diphenoxylate/atropine, and octreotide.

Laboratory studies are shown below.

Stool studies are negative for infectious agents.

Which of the following therapeutic agents should be considered in this patient to reduce his episodes of dehydration?

- A. Cholestyramine
- B. Dicyclomine
- C. Teduglutide
- D. Magnesium oxide

CORRECT ANSWER: C

RATIONALE

This patient has short bowel syndrome and suffers from intermittent dehydration from severe diarrhea, which results in electrolyte disturbances. He would benefit from additional medical therapy to reduce his diarrhea. Due to the large amount of ileum resected, his bile salt pool is low; therefore, cholestyramine would not be appropriate because it would further deplete his already low bile salt pool and cause steatorrhea. Dicyclomine can slow gut

Laboratory Test	Result	Reference Range
Bicarbonate, serum, mEq/L	18	23-28
Blood urea nitrogen (BUN), serum or plasma, mg/dL	28	8-20
Chloride, serum, mEq/L	109	98-106
Creatinine, serum, mg/dL	1.5	0.7-1.5
Glucose, plasma (fasting), mg/dL	92	70-99
Magnesium, serum, mEq/L	1.4	1.6-2.6
Potassium, serum, mEq/L	3.0	3.5-5.0
Sodium, serum, mEq/L	136	136-145

transit but is unlikely to substantially reduce his severe diarrhea. Magnesium oxide, though a treatment of hypomagnesemia, can cause diarrhea as a side effect. The correct answer is teduglutide, which is a glucagon-like peptide-2 analogue that improves intestinal absorption of fluids and nutrients; it is approved by the US Food and Drug Administration for patients with short gut syndrome.

REFERENCE

Jeppesen PB, Pertkiewicz M, Messing B, et al. Teduglutide reduces need for parenteral support among patients with short bowel syndrome with intestinal failure. *Gastroenterology*. 2012;143(6):1473-1481.e3. doi:10.1053/j.gastro.2012.09.007

Question 13

You are called to see a 28-year-old woman in your hospital’s emergency department for hematemesis. She developed sudden-onset hematemesis approximately 2 hours after her dinner at home last night. She denies sick contacts and does not drink alcohol or use illicit drugs. She has no significant past medical history and has never had any surgeries. She does recall having a similar episode a few years ago for which she underwent endoscopic evaluation at an outside hospital, but she does not recall the results. The remainder of her review of systems is negative. On examination, she appears comfortable and in no apparent distress. Her vital signs reveal a normal temperature, blood pressure of 102/68 mmHg, heart rate of 102 bpm, and normal oxygen saturation. Her body mass index is 20 kg/m². Head and neck examination is remarkable for poor dentition; cardiopulmonary and abdominal examinations are normal. Evaluation reveals the laboratory values listed below.

You perform in upper endoscopy which reveals Los Angeles grade B esophagitis and a Mallory Weiss tear. The remainder of the examination is unremarkable.

Which of the following is the most likely diagnosis?

- A. Eosinophilic esophagitis
- B. Idiopathic gastroparesis
- C. Binge eating disorder
- D. Bulimia nervosa
- E. Cyclic vomiting syndrome

CORRECT ANSWER: D

RATIONALE

This patient is presenting with an upper gastrointestinal bleed secondary to a Mallory Weiss tear resulting from purging behavior. Bulimia nervosa is an eating disorder characterized by binge eating coupled with compensatory behaviors to prevent weight gain. The compensatory behavioral changes can be purging, laxative abuse, or excessive exercise. Complications of bulimia nervosa include dental caries, erosive esophagitis, diarrhea, electrolyte disturbances, and Mallory Weiss tears as seen in this patient. Binge eating disorder is a possible diagnosis in this patient; however, patients with binge eating disorder typically are overweight or obese because they do not have compensatory mechanisms to prevent weight gain. Cyclic vomiting syndrome is not the most likely diagnosis in this case considering all the other information supporting bulimia nervosa.

REFERENCE

Harrington BC, Jimerson M, Haxton C, Jimerson DC. Initial evaluation, diagnosis, and treatment of

Laboratory Test	Result	Reference Range
Blood urea nitrogen (BUN), serum or plasma, mg/dL	30	8-20
Chloride, serum, mEq/L	104	98-106
Creatinine, serum, mg/dL	0.7	0.7-1.5
Hemoglobin, blood, g/dL	11.5	14-18
Mean corpuscular volume, fL	78	80-98
Potassium, serum, mEq/L	3.9	3.5-5.0
Sodium, serum, mEq/L	135	136-145

anorexia nervosa and bulimia nervosa. *Am Fam Physician*. 2015;91(1):46-52.

Question 14

Which of the following hormonal responses is consistently seen after bariatric surgery?

- A. Decreased cholecystokinin (CCK)
- B. Increased glucagon-like peptide-1 (GLP-1)
- C. Decreased peptide YY (PYY)
- D. Increased ghrelin

CORRECT ANSWER: B

RATIONALE

Bariatric surgery is the most effective, durable treatment for obesity. Bariatric surgeries can be restrictive and/or malabsorptive and alter the handling of ingested nutrients. Bariatric surgeries have also been shown to alter circulating levels of gut-derived hormones that play a role in hunger and satiety, such as ghrelin, GLP-1, CCK and PYY. It has been shown that after sleeve gastrectomy and Roux-en-Y gastric bypass, serum levels of GLP-1, CCK and PYY are increased. GLP-1, secreted from L-cells in the distal small intestine and colon, stimulates insulin secretion, inhibits glucagon as well as gastrointestinal secretions and motility. CCK, produced by intestinal I-cells, is a satiety hormone and inhibits gastric motility. The effect of bariatric surgery on ghrelin is not as clear; some data shows the levels increase, while others show ghrelin decreases due to the weight loss.

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Quercia I, Dutia R, Kotler DP, Belsley S, Laferrère B. Gastrointestinal changes after bariatric surgery. *Diabetes Metab*. 2014;40(2):87-94. doi:10.1016/j.diabet.2013.11.003

Tuero C, Valenti V, Rotellar F, Landecho MF, Cienfuegos JA, Frühbeck G. Revisiting the Ghrelin Changes Following Bariatric and Metabolic Surgery. *Obes Surg*. 2020;30(7):2763-2780. doi:10.1007/s11695-020-04601-5

Question 15

You see a 61-year-old man with a history of chronic, alcohol-related pancreatitis complicated by pancreatic insufficiency in follow-up. Since his last visit, he has been well and reports loose, non-bloody postprandial stools and 2 pounds of weight loss. In addition, he has moderate flank pain for which he was seen in his local urgent care and diagnosed with a musculoskeletal strain. Although you prescribed him pancreatic enzyme replacement therapy, he frequently forgets to take it. A pancreas protocol computed tomography shows pancreatic calcifications and atrophy but no mass lesion in the pancreas. You counsel the patient on the importance of adherence to pancreatic enzyme replacement therapy citing which of the following possible complications of untreated, chronic pancreatic insufficiency?

- A. Pancreatic adenocarcinoma
- B. Oxalate nephrolithiasis
- C. Gastroparesis
- D. Peptic ulcer disease

CORRECT ANSWER: B

RATIONALE

Secondary hyperoxaluria leading to oxalate nephrolithiasis can occur in patients with fat maldigestion and fat malabsorption. As a result of the preferential binding of calcium to fat, unbound oxalate is absorbed in the colon and can alternately lead to the formation of oxalate stones. Patients with chronic pancreatic insufficiency and associated steatorrhea have an increased risk of oxalate stones, though this is not commonly reported in the literature. Other conditions that may predispose to secondary hyperoxaluria from fat malabsorption include ileal resection in the setting of malignancy or inflammatory bowel disease, bariatric surgery, and use of the weight loss drug orlistat, which is a lipase inhibitor.

REFERENCE

Cartery C, Faguer S, Karras A, et al. Oxalate nephropathy associated with chronic pancreatitis. *Clin J Am Soc Nephrol*. 2011;6(8):1895-1902. doi:10.2215/CJN.00010111

Demoulin N, Aydin S, Gillion V, Morelle J, Jadoul M. Pathophysiology and Management of Hyperoxaluria and Oxalate Nephropathy: A Review [published online ahead of print, 2021 Sep 9]. *Am J Kidney Dis*. 2021;S0272-6386(21)00834-9. doi:10.1053/j.ajkd.2021.07.018

Question 16

You are asked to see a 76-year-old nursing home resident who has a clogged gastrostomy tube (G tube). The tube was functioning properly until the nurse noted difficulty with flushing it before medication administration. The staff has tried unclogging the tube with warm water without success. The patient is nonverbal and unable to provide any history. On examination, the patient is afebrile with stable vital signs. A focused abdominal examination reveals a soft, nondistended abdomen. The patient grimaces slightly with palpation around the tube. The tube appears to be a balloon-tipped G tube; however, the external markings on the tube are not visible. You are unable to advance or rotate the tube without resistance.

The stoma site has mild erythema and serous drainage, but no fluctuance is noted. Based on your clinical suspicion for the underlying etiology, which of the following is the best next step?

- A. Schedule endoscopy for replacement of the tube
- B. Instill Coca-Cola into the tubing to declog it
- C. Attempt to declog using a tube-cleaning brush
- D. Instill air into the tube's balloon
- E. Treat with a 7-day course of antibiotics

CORRECT ANSWER: A

RATIONALE

The patient has buried bumper syndrome. Buried bumper syndrome may present with abdominal pain, drainage at the tube site, or clogging of

the tube. The management for buried bumper is removal and replacement of the tube.

REFERENCE

Sealock RJ, Munot K. Common Gastrostomy Feeding Tube Complications and Troubleshooting. *Clin Gastroenterol Hepatol*. 2018;16(12):1864-1869. doi:10.1016/j.cgh.2018.07.037

Question 17

Which of the following interventions is recommended to reduce the risk of central line-associated bloodstream infections (CLABSI) in patients receiving long-term central parental nutrition (PN)?

- A. Continuous PN infusion
- B. Multiple lumen central catheters
- C. Soy bean, medium-chain triglyceride, olive oil, fish oil lipid emulsion
- D. Tunneled central catheters

CORRECT ANSWER: D

RATIONALE

The 2018 guidelines published by the American Society of Parenteral and Enteral Nutrition recommend tunneled central venous catheters for adult patients anticipated to require long-term daily PN infusions. Central venous catheters with multiple lumens have been shown to be associated with higher infection risk; thus, fewer lumens are recommended. Alternative lipid emulsions are not associated with lower CLABSI risk. Continuous parenteral nutrition infusion is associated with increased risk of PN-related cholestasis, not a lower risk of CLABSIs.

REFERENCES

Gundogan K, Dave NJ, Griffith DP, et al. Ethanol Lock Therapy Markedly Reduces Catheter-Related Blood Stream Infections in Adults Requiring Home Parenteral Nutrition: A Retrospective Study From a Tertiary Medical Center. *JPEN*

J Parenter Enteral Nutr. 2020;44(4):661-667. doi:10.1002/jpen.1698

Kovacevich DS, Corrigan M, Ross VM, McKeever L, Hall AM, Braunschweig C. American Society for Parenteral and Enteral Nutrition Guidelines for the Selection and Care of Central Venous Access Devices for Adult Home Parenteral Nutrition Administration. *JPEN J Parenter Enteral Nutr.* 2019;43(1):15-31. doi:10.1002/jpen.1455

Lai NM, Chaiyakunapruk N, Lai NA, O’Riordan E, Pau WS, Saint S. Catheter impregnation, coating or bonding for reducing central venous catheter-related infections in adults. *Cochrane Database Syst Rev.* 2016;3(3):CD007878. Published 2016 Mar 16. doi:10.1002/14651858.CD007878.pub3

Question 18

Which of the following demographic groups has the greatest risk of metabolic complications at a lower body mass index (BMI)?

- A. Non-Hispanic Black
- B. Non-Hispanic White
- C. Hispanic
- D. Non-Hispanic Asian

CORRECT ANSWER: D

RATIONALE

Studies show racial and ethnic disparities with respect to obesity prevalence as well as obesity-related comorbid conditions. In White populations, increased mortality is seen in the extremes of BMI (low and high BMI). Mortality is the lowest in normal BMI individuals, whereas an increase in mortality is noted at a BMI greater than 25 kg/m². The increase in mortality occurs at a higher BMI in Black populations (BMI of 32-33 kg/m² for men and BMI of 37-38.77 kg/m² for women). Studies show that in Asian populations, metabolic complications of obesity occur at a BMI of 23 kg/m² to 24.78 kg/m², which is

considered within the normal BMI range. This phenomenon enforces the notion that BMI is not the optimal metabolic risk assessment method in all populations. Understanding obesity disparities is particularly important for gastroenterologists because of the potential implications on the recommendation for, and implementation of, weight reduction strategies.

REFERENCES

Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of Obesity Among Adults and Youth: United States, 2015-2016. *NCHS Data Brief.* 2017;(288):1-8.

WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet.* 2004;363(9403):157-163. doi:10.1016/S0140-6736(03)152683

Question 19

An 18-year-old woman with anorexia nervosa is admitted to a local hospital for severe protein-calorie malnutrition. She is begun on enteral nutrition support providing 75% of her energy needs via nasogastric tube. On hospital day 3, she is emergently transferred to the intensive care unit with acute shortness of breath and found to be in cardiogenic shock.

What is the most likely electrolyte disturbances do you expect a patient with this condition to have?

- A. Hyperkalemia
- B. Hypophosphatemia
- C. Hyponatremia
- D. Hypercalcemia
- E. Hypermagnesemia

CORRECT ANSWER: B

RATIONALE

Refeeding syndrome is a condition character-

ized by acute volume overload associated with electrolyte disturbances due to an abrupt increase in phosphate needs. At-risk patients may become severely hypophosphatemic, hypokalemic, and/or hypomagnesemic as the body recruits minerals from all compartments. Serious consequences of refeeding syndrome can include acute pulmonary edema, congestive heart failure, and sudden cardiac death. Patients with anorexia are at high risk for refeeding syndrome, and should be started on 25% of energy needs.

REFERENCE

Friedli N, Stanga Z, Sobotka L, et al. Revisiting the refeeding syndrome: Results of a systematic review. *Nutrition*. 2017;35:151-160. doi:10.1016/j.nut.2016.05.016

Question 20

In a patient with short bowel syndrome, which of the following reflects the optimal composition of an oral hydration solution?

- A. Hypotonic, low sodium:glucose ratio
- B. Hypertonic, low sodium:glucose ratio
- C. Isotonic, high sodium:glucose ratio
- D. Isotonic, low sodium:glucose ratio

CORRECT ANSWER: C

RATIONALE

The mechanism of oral hydration solutions is dependent on the jejunal sodium-glucose energy dependent co-transport system. Solutions that leverage this transport system optimize sodium absorption in an effort to maintain a stable hydration status. In individuals who have short bowel syndrome and reduced intestinal absorptive capacity, hypotonic solutions result in water secretion from the bowel, thus, increasing fecal water output. Similarly hypertonic solutions result in secretion of water and increased fecal output. An isotonic solution with a low sodium to glucose ratio would not maximize the sodium-glucose cotransporter mechanism; therefore, the optimal

oral hydration solution should be isotonic with a higher sodium:glucose ratio.

REFERENCE

Atia AN, Buchman AL. Oral rehydration solutions in non-cholera diarrhea: a review. *Am J Gastroenterol*. 2009;104(10):2596-2605. doi:10.1038/ajg.2009.329

Question 21

A 57-year-old man with fistulizing Crohn disease comes in for a follow-up visit. He reports reduced appetite and a 15-pound weight loss in the past 6 months. He reports 2 to 3 non-bloody bowel movements daily, but he denies abdominal pain, nausea or vomiting. On examination, he appears comfortable, height of 1.7 m, weight of 61.6 kg, and body mass index of 22 kg/m². You note fat wasting in the temporal areas, and he has good muscle bulk.

Which of the following describes this patient's nutritional status based on your assessment?

- A. Well nourished, low nutritional risk
- B. Mild malnutrition, mild-moderate nutritional risk
- C. Severe malnutrition, high nutritional risk
- D. Mild malnutrition, low nutritional risk

CORRECT ANSWER: B

RATIONALE

This patient has clinically significant (10% of baseline weight) weight loss in the context of active, ongoing inflammatory disease. He also has had altered oral intake and due to his diarrhea has altered nutrient absorption. On examination, he has fat wasting as well.

This patient has mild evidence of malnutrition on examination with fat wasting, but he has no muscle mass loss or edema that are indicators of severe malnutrition. Because of his weight loss and active ongoing inflammation, he is at increased nutri-

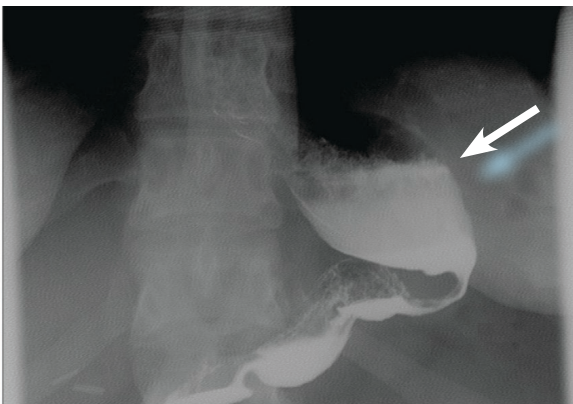
tional risk. There are numerous published nutrition assessment tools; however, weight changes, altered oral intake, and physical examination findings such as fat and muscle wasting and ascites are often included and used to differentiate patients who are either well nourished, mild-moderately malnourished, or severely malnourished.

REFERENCE

White JV, Guenter P, Jensen G, et al. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *J Acad Nutr Diet*. 2012;112(5):730-738. doi:10.1016/j.jand.2012.03.012

Question 22

A 48-year-old man presents for evaluation of regurgitation. He underwent laparoscopic sleeve gastrectomy 8 years ago and did well with loss of 75% of his excess body weight. He did well until 3 years ago when he sustained injuries in a motor vehicle accident and was immobile during his prolonged recovery period; he gained back a good amount of his weight lost. You perform an upper endoscopy that reveals normal sleeve gastrectomy anatomy without stricture and mild mucosal erythema. You order an upper gastrointestinal barium study, which is shown below.



Ma IT, Madura JA. *Gastroenterol Hepatol (N Y)*. 2015;11(8):526-535

What is the most likely underlying etiology of the patient's symptoms and the findings on the upper gastrointestinal study?

- A. Gastric ulcer
- B. Weight regain
- C. Nonadherence to proton pump inhibitors
- D. Gastric cancer
- E. Hiatus hernia

CORRECT ANSWER: B

RATIONALE

Following sleeve gastrectomy, the luminal caliber of the stomach can dilate over time, especially in the setting of overeating, and can sometimes lead to the development of a "neofundus." This dilated "neofundus" can contribute to further weight gain due to increased gastric accommodation and consumption of larger volumes of food. Patients can also develop symptoms of regurgitation, heart-burn, and abdominal pain. In addition, the dilated proximal stomach and the appearance of a relative mid-stomach stenosis/stricture (as seen on the image above) with subsequent food stasis can also lead to symptoms of gastroesophageal reflux. There is no significant stricture, as this would be noted on endoscopy. No gastric ulcer, gastric cancer or hiatal hernia is seen on endoscopy or barium.

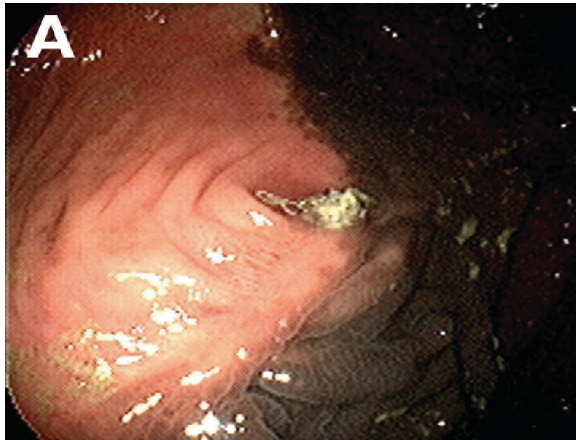
REFERENCE

Ma IT, Madura JA 2nd. Gastrointestinal Complications After Bariatric Surgery. *Gastroenterol Hepatol (N Y)*. 2015;11(8):526-535.

Question 23

A 19-year-old presents with her parents for evaluation of chronic diarrhea. They report up to 6 non-bloody, watery bowel movements daily and associated 10-pound weight loss. There is no prior history of constipation or abdominal pain. Stool studies for enteric pathogens including *Clostridioides difficile* are negative. She has a family history of Crohn disease in her maternal uncle. She denies alcohol and tobacco use or illicit drug use and is a competitive

gymnast. She is a college sophomore and reports academic pressures and those from her sport. On examination, she is a well-appearing woman with a muscular build. Serologic testing for celiac disease is negative. You perform a colonoscopy with terminal ileal intubation. The images from the colonoscopy are shown below.



Li D, Browne LW, Ladabaum U. 2009;7(9):A20. doi:10.1016/j.cgh.2008.11.030

Which of the following pathologic findings are most likely in this patient?

- A. Noncaseating granulomas
- B. Subepithelial collagen band
- C. Subepithelial lymphocytosis
- D. Periodic acid–Schiff stain with pigment-laden macrophages
- E. Abundant mucosal eosinophils

CORRECT ANSWER: D

RATIONALE

The endoscopic appearance of this patient's colonoscopy is consistent with melanosis coli. The characteristic pathologic finding in melanosis coli is pigment-laden macrophages noted on periodic acid–Schiff staining. Melanosis coli is associated with chronic laxative use and can be seen in patients with chronic constipation who use laxatives, in those with surreptitious use for a secondary gain, or in patients with eating disorders such

as anorexia or bulimia nervosa. Laxative abuse among the latter group reportedly ranges from 10% to 60%. This patient's diarrhea evaluation has been essentially unremarkable with no evidence of infectious causes or inflammatory bowel disease to explain her diarrhea. Laxative abuse has also been described by those engaged in competitive sports where there are set weight limits that impose guidelines to maintain a specific weight. Recognizing laxatives abuse and the potential link to an underlying eating disorder is critical to preventing excessive diagnostic testing and ultimately referring the patient for appropriate interventions.

REFERENCES

Li D, Browne LW, Ladabaum U. Melanosis coli. *Clin Gastroenterol Hepatol*. 2009;7(9):A20. doi:10.1016/j.cgh.2008.11.030

Roerig JL, Steffen KJ, Mitchell JE, Zunker C. Laxative abuse: epidemiology, diagnosis and management. *Drugs*. 2010;70(12):1487-1503. doi:10.2165/11898640-000000000-00000

Question 24

A 40-year-old woman with a history of sicca syndrome and chronic idiopathic pancreatitis presents for evaluation of bloating. She reports that her symptoms are linked to meals and cause abdominal discomfort due to distension. She was advised to eat a low-fat diet, which she adheres to, and she reports that her diet is rich in starchy foods such as rice, pasta, and bread. She avoids carbonated beverages. She does report some mild diarrhea, but her weight has been stable. She has not traveled or taken antibiotics in the recent past.

On examination, she appears comfortable, is afebrile, and has normal vital signs. Abdominal examination reveals mild abdominal distension and tympany to percussion. Her evaluation reveals normal celiac serologies. Stool studies are negative for *Giardia* and show a low pancreatic elastase. A magnetic resonance imaging of the abdomen and pelvis does not reveal a pancreatic mass. Her

upper endoscopy was unremarkable with normal duodenal biopsies.

Which of the following is the most likely pathophysiologic mechanism driving her bloating?

- A. Reduced pancreatic lipase
- B. Reduced salivary and pancreatic amylase
- C. Reduced gastric and pancreatic lipase
- D. Increased gastric acid

CORRECT ANSWER: B

RATIONALE

This patient's bloating symptoms are due to carbohydrate maldigestion resulting from reduced salivary and pancreatic amylase. Carbohydrate digestion begins with hydrolysis of polysaccharides by salivary and pancreatic amylase to oligo and disaccharides, which are then hydrolyzed into monosaccharides by brush border enzymes that are ultimately absorbed across the intestinal mucosa. Salivary amylase is reduced in patients with sicca syndrome and pancreatic amylase can be reduced in patients with chronic pancreatitis with pancreatic insufficiency, which can lead to carbohydrate maldigestion. Carbohydrate maldigestion can present with bloating, abdominal pain, and diarrhea. Although the patient is at risk for pancreatic insufficiency, she does not have symptoms of fat maldigestion because she adheres to a low-fat diet.

REFERENCES

Kiela PR, Ghishan FK. Physiology of Intestinal Absorption and Secretion. *Best Pract Res Clin Gastroenterol*. 2016;30(2):145-159. doi:10.1016/j.bpg.2016.02.007

Olesen SS, Krarup H, Poulsen JL, et al. Pancreas-specific plasma amylase for assessment and diagnosis of chronic pancreatitis: New insights on an old topic. *United European Gastroenterol J*. 2019;7(7):955-964. doi:10.1177/2050640619846011

Question 25

Which of the following food sensitivity syndromes would most likely have a positive serum IgE and skin prick test?

- A. Celiac disease
- B. Nonceliac gluten sensitivity
- C. Oral allergy syndrome
- D. Lactose intolerance
- E. Protein-induced enterocolitis or enteropathy syndromes

CORRECT ANSWER: C

RATIONALE

Food sensitivities can be IgE-, non-IgE-, or mixed IgE-mediated. Of the options provided, oral allergy syndrome is the only IgE-mediated condition and would likely have a positive serum IgE based test and/or skin prick testing. Celiac disease and protein-induced enterocolitis or enteropathy syndromes are both considered non-IgE-based conditions. Nonceliac gluten sensitivity is not considered to be an immune-mediated condition.

REFERENCE

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Question 26

A 25-year-old woman presents with 3 months of diarrhea and bloating that are worse after eating. She denies abdominal pain or any weight loss. On physical examination, her weight is 55 kg, and her body mass index is 20.1 kg/m² with normal vital signs. She has a normal body habitus but with mild pallor of the conjunctivae. Her abdomen is mildly tympanic to percussion but is otherwise nontender to palpation.

Laboratory findings are shown on the following page.

Laboratory Test	Result	Reference Range
Anti-tissue transglutaminase IgA, U/mL	45	0-15
Ferritin, serum, ng/mL	124	24-307
Folate, serum, ng/mL	10	1.8-9.0
Hemoglobin, blood, g/dL	11.8	12-16
IgA, mg/dL	200	90-325
Mean corpuscular volume, fL	80	80-98
Vitamin B ₁₂ , serum, pg/mL	412	200-800

You order an upper endoscopy with duodenal biopsies to confirm celiac sprue, but these come back normal.

Which of the following should you do next?

- A. Conduct no further testing as this is a false positive serology, and she likely has irritable bowel syndrome
- B. Place her on a high-gluten diet for 6 weeks, then repeat an endoscopy with more duodenal biopsies
- C. Schedule a hydrogen breath test to evaluate for small intestinal bacteria overgrowth
- D. Perform a video capsule endoscopy to evaluate her entire small intestine
- E. Check for an anti-endomysial or anti-deamidated gliadin peptide antibody

CORRECT ANSWER: E

RATIONALE

False positive celiac serologies using anti-tissue transglutaminase IgA antibodies are rare given the high specificity of this test, but when they do occur, the elevation is low titer (typically less than twice the upper limit of normal). In this case, her test result is 3 times the upper limit of normal. Since celiac sprue can be patchy in the duodenum, histology may be normal. When the initial serology test and the duodenal histology results are discordant, the first thing to do is either check an alternative serologic test such as anti-endomysial-IgA or anti-deamidated gliadin peptide-IgG antibodies since these are highly specific (close to 100% specificity). Alternatively, you can measure human leukocyte antigen DQ2/DQ8 genotypes given the negative predictive value of these are

greater than 99%. Since these tests are less invasive, they should be performed first before embarking on a formal gluten challenge with repeat biopsies. Given the normal vitamin B₁₂ and folate, small intestinal bacteria overgrowth is less likely and still would not explain the elevated anti-tissue transglutaminase IgA antibody. A video capsule endoscopy would not add more information in this case.

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Question 27

A 45-year-old man with pan-ulcerative colitis and associated arthropathy sees you for a routine office visit. He has been on oral sulfasalazine 1 gram 3 times daily for the past 18 months and is in clinical and endoscopic remission. He denies any further diarrhea or rectal bleeding and his abdominal and joint pains have completely resolved since a year ago. However, his energy levels remain low. His vital signs are normal, but on physical examination he has a reddened, smooth tongue. A C-reactive protein and fecal calprotectin are both normal correlating with his symptom resolution.

What nutrient deficiency is the most likely and what is its mechanism?

- A. Vitamin B₁₂ deficiency due to backwash ileitis
- B. Folate deficiency due to sulfasalazine use
- C. Vitamin D deficiency due to fat malabsorption
- D. Iron deficiency due to a history of rectal bleeding
- E. Zinc deficiency due to excessive losses from diarrhea

CORRECT ANSWER: B

RATIONALE

Sulfasalazine is a competitive inhibitor of folate absorption; therefore, folic acid should be supplemented while taking this medication. Folate deficiency can lead to a macrocytic anemia, which can cause fatigue. Although glossitis can also occur in vitamin B₁₂ deficiency, this vitamin's absorption is unaffected by sulfasalazine use. Additionally, he does not have terminal ileal inflammation as this is ulcerative colitis rather than Crohn's disease, so there is no reason for vitamin B₁₂ deficiency. Iron deficiency can also cause glossitis, but he has not had any rectal bleeding for over 1 year. Fat soluble vitamin malabsorption (vitamin D) would not occur due to colitis.

REFERENCE

Wani NA, Hamid A, Kaur J. Folate status in various pathophysiological conditions. *IUBMB Life*. 2008;60(12):834-842. doi:10.1002/iub.133

Question 28

A 51-year-old man is currently admitted to the hospital for high ostomy output for which you are consulted. He has been on home total parenteral nutrition (TPN) for the last 18 months after he had his colon and most of his small intestine removed due to trauma. He has an end jejunostomy present that is 80 cm past the ligament of Treitz and has been having between 5 to 6 liters of ostomy output daily despite using octreotide and codeine. His TPN provides 2000 kcal daily in 2.3 L of dextrose,

lipids, and amino acids plus standard amounts of electrolytes, vitamins, and minerals. Vital signs show a resting heart rate of 114 bpm and a blood pressure of 110/90 mmHg. On physical examination, he has elevated jugular venous pressure and diffuse 3/5 muscle weakness.

Which of the following micronutrient deficiencies does the patient most likely have?

- A. Zinc
- B. Manganese
- C. Selenium
- D. Copper
- E. Chromium

CORRECT ANSWER: C

RATIONALE

Selenium deficiency causes muscle weakness and fatigue and can lead to cardiomyopathy resulting in congestive heart failure. This patient has weakness on examination as well as signs of congestive heart failure. Although selenium is added to TPN, often it may not be enough to compensate for the elevated selenium needs that occur in states of malabsorption such as in the case of short bowel syndrome. Zinc and manganese deficiencies instead lead to night blindness as well as confusion. Encephalopathy and peripheral neuropathy can occur in copper and chromium deficiencies. Although copper deficiency can also cause muscle weakness, it is not responsible for cardiomyopathy.

REFERENCE

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Question 29

A 28-year-old woman presents with ongoing intermittent diarrhea and bloating for the past 2 years. She has had a thorough workup, which

has included a normal anti-tissue transglutaminase IgA antibody, vitamin B₁₂, folate, as well as a normal random quantitative fecal fat and ova and parasites. In addition, she has had an upper endoscopy and colonoscopy with duodenal, ileal, and colonic biopsies, which all returned normal. You diagnosed her with irritable bowel syndrome and recommended symptom management. Since your last visit with her, a friend suggested she try a gluten-free diet, which she has begun and has noticed some improvement in her symptoms. She now asks if she has gluten intolerance.

What is the most likely explanation to her symptomatic improvement?

- A. She has also reduced fructans in her diet resulting in less ingestion of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols
- B. She has seronegative celiac sprue that is responding to a strict gluten-free diet
- C. She has an IgE-mediated wheat allergy that has been causing her symptoms
- D. She has a protein-induced enterocolitis from gluten
- E. She has eosinophilic colitis caused by gluten

CORRECT ANSWER: A

RATIONALE

The clinical entity of nonceliac gluten sensitivity or gluten intolerance has been defined as those without celiac disease but whose gastrointestinal symptoms improve on a gluten-free diet. However, the presence of other components of wheat, particularly fructans, have previously not been considered as the actual culprit behind a patient's symptoms. A study done by Biesiersky et al demonstrated that when patients previously found to be gluten sensitive had FODMAPS (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) eliminated from their diet, re-introduction of wheat-poor gluten did not induce gluten-specific symptoms. This supports the notion that gluten is not responsible for diar-

rhea and bloating in patients without celiac sprue. Given her celiac serologies and duodenal biopsies were both negative, this effectively rules out celiac sprue. An IgE-mediated allergy would typically cause cutaneous symptoms, wheezing, or angioedema in adults and not intestinal symptoms. If diarrhea does occur, it happens immediately after eating. Food protein-induced enterocolitis is generally a condition seen in childhood; however, it can rarely occur in adults, but the allergen is proteins found in mollusks and shellfish, not gluten. Lastly, her colonic biopsies were negative for any eosinophils, which rules out eosinophilic colitis.

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Question 30

A 56-year-old man comes to see you in your office for chronic heartburn for which he has taken omeprazole 20 mg once daily for the past 10 years. Although his heartburn is well controlled, he has noticed that things do not taste as well as they used to. He denies any regurgitation, nausea, or vomiting. He also denies any impairment to his sense of smell or xerostomia. On examination, he has normal oral mucosa without any aphthae. He has no rashes on his skin and his neurologic examination is also normal. Recent laboratory values are shown at the top on the following page.

Laboratory Test	Result	Reference Range
Calcium, serum, mg/dL	9.7	8.6–10.2
Hemoglobin, blood, g/dL	14.9	14–18
Magnesium, serum, mEq/L	2.1	1.6–2.6

He had an upper endoscopy last year to screen for Barrett's esophagus, which was also normal without any evidence of erosive esophagitis or intestinal metaplasia.

Which of the following nutrient deficiencies is the most likely cause for his dysgeusia?

- A. Phosphorus
- B. Vitamin C
- C. Zinc
- D. Vitamin B₁₂
- E. Iron

CORRECT ANSWER: C

RATIONALE

Dysgeusia, or altered taste, is a well-described side effect of zinc deficiency. Although not fully understood, it is believed that zinc is partially responsible for the repair and production of taste buds. Zinc losses can occur in those with diarrhea, but there are studies that show proton pump inhibitors can interfere with zinc absorption as well. Checking a zinc level or empirically treating with zinc supplements would be a reasonable next step here. Chronic phosphorus deficiency typically leads to muscle weakness, particularly of the eye muscles, and is generally seen in those with hyperparathyroidism or on long-term diuretics. Vitamin C deficiency can cause a burning sensation in the mouth and bleeding gums but does not impair taste. Vitamin B₁₂ deficiency is known to cause neurologic symptoms and a macrocytic anemia; however, this patient has a normal hemoglobin.

Iron deficiency also causes anemia, although a microcytic one, and sufferers may also crave or chew substances of no nutritional value (eg ice), which this patient is not.

REFERENCES

Farrell CP, Morgan M, Rudolph DS, et al. Proton Pump Inhibitors Interfere With Zinc Absorption and Zinc Body Stores. *Gastroenterology Res.* 2011;4(6):243-251. doi:10.4021/gr379w

Mason JB. Genetic Disorders of the Pancreas and Pancreatic Disorders in Childhood. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*, 11th ed. Elsevier, Inc; 2020:52-73.

Question 31

A 45-year-old man presents to your office for a new visit regarding intermittent nausea, vomiting, and diarrhea. This has been going on for the last 6 months with no clear pattern, although he thinks it tends to happen after eating dairy products or hotdogs. Each episode lasts 6 to 8 hours and afterwards he feels warm and flushed. He denies any allergic symptoms such as hives, wheezing, or swelling. His past medical history is only notable for mild exercise-induced asthma. He denies any dysphagia, heartburn, or early satiety. He has tried diphenhydramine, famotidine, bismuth, and peppermint oil after each episode with some symptomatic relief. His vital signs are normal, as is his physical examination. Laboratory analysis shows the following:

Laboratory Test	Result	Reference Range
5-Hydroxyindoleacetic acid, urine, mg/24 hours	2.5	0.0–14.9
Alpha-gal IgE, kU/L	<0.1	<0.1
Serotonin, serum, ng/mL	60	50–200
Tryptase, serum, ng/mL	30.2	1–14

An upper endoscopy is performed with normal gastric and duodenal biopsies.

Which is the most likely condition to explain his symptoms?

- A. Carcinoid syndrome
- B. Mast cell activation disorder
- C. Alpha-gal allergy
- D. Scombroid poisoning
- E. Eosinophilic gastroenteritis

CORRECT ANSWER: B

RATIONALE

When flushing is experienced with intermittent episodes of nausea, vomiting, diarrhea, and/or abdominal pain, typically an IgE-, serotonin-, or histamine-mediated response is taking place. Serum tryptase levels are elevated in mast cell activation disorders, which are due to the inappropriate release of histamine, often in response to certain foods, such as dairy, sulfites (preservatives frequently found in hotdogs), and alcohol. Criteria for this condition includes symptoms of histamine release, evidence of mast cell involvement demonstrated with an elevated serum tryptase, and symptomatic response to antihistamines. This patient has demonstrated all 3 criteria; therefore, a mast cell activation disorder explains his symptoms.

In carcinoid syndrome, serum serotonin and 24-hour urine 5hydroxyindoleacetic acid levels are elevated due to the presence of an underlying neuroendocrine tumor with liver metastases. Alpha-Gal allergy or mammalian meat allergy is due to an IgE-mediated response to the non-primate, mammalian carbohydrate galactose-alpha-1,3-galactose, contracted after a bite from the lone star tick, *Amblyomma americanum*. Typically, this develops after ingestion of beef or pork products, and although he has noticed a pattern to dairy and pork products, he has a normal alpha-gal IgE level. Scombroid poisoning occurs after eating spoiled fish (typically tuna or mackerel) that contain high amounts

of histamine. However, serum tryptase levels are normal in this condition. Lastly, eosinophilic gastroenteritis would demonstrate high amounts of eosinophils (>30 eosinophils/high-power field/mm²) throughout the stomach and small intestine, which this patient does not have.

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Stratta P, Badino G. Scombroid poisoning. *CMAJ.* 2012;184(6):674. doi:10.1503/cmaj.111031

Question 32

An 81-year-old woman with coronary artery disease on daily aspirin presents to your office for her annual visit. She has been taking a prescription-strength proton pump inhibitor once daily for the last 3 years after she developed a gastric ulcer bleed. She denies any abdominal pain, heartburn, or reflux, but has recently been diagnosed with mild dementia and found to be anemic. Physical examination reveals angular stomatitis and decreased sensation to pain in the lower extremities. Recent laboratory tests performed by her primary care physician are shown at the top of the following page.

Laboratory Test	Result	Reference Range
Folate, serum, ng/mL	14.6	1.8–9.0
Hemoglobin, blood, g/dL	9.7	12–16
Leukocyte (WBC) count, cells/ μ L	9000	4000–11,000
Mean corpuscular volume, fL	106	80–98
Platelet count, plt/μ L	251,000	150,000–450,000
Vitamin B ₁₂ , serum, pg/mL	94	200–800

You perform a repeat upper endoscopy and colonoscopy to evaluate her anemia, and although her colon is normal, she does have moderate atrophic gastritis seen on histology.

Which of the following statements applies to this patient?

- A. Oral supplementation of vitamin B₁₂ should be started right away
- B. Vitamin B₁₂ deficiency would not explain her loss of pain sensation
- C. A common cause of vitamin B₁₂ deficiency is chronic aspirin use
- D. Vitamin B₁₂ deficiency is a result of antibodies to intrinsic factor
- E. Proton pump inhibitor use is unrelated to vitamin B₁₂ deficiency

CORRECT ANSWER: D

RATIONALE

Pernicious anemia (PA) is the most common cause of vitamin B₁₂ deficiency and occurs as a result of autoantibodies to parietal cells and/or to intrinsic factor. This results in decreased production of intrinsic factor or a decrease in vitamin B₁₂ absorption in the terminal ileum. PA is thought to be the end stage of an autoimmune process that results in severe damage of the oxyntic gastric mucosa, which appears atrophic on histology. *Helicobacter pylori* infection and prolonged proton pump inhibitor use can also result in vitamin B₁₂ deficiency due to a decrease in vitamin B₁₂ release from food as a result of a hypochlorhydric state. However, chronic aspirin use has not been found to cause vitamin B₁₂ deficiency. Vitamin B₁₂ deficiency causes neuropsy-

chiatric changes including a decrease in cognition and a loss of pain sensation in the lower extremities. Although oral replacement of vitamin B₁₂ has been shown effective even in PA, due to the presence of neurologic deficits, intramuscular injections should be started first.

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Langan RC, Goodbred AJ. Vitamin B₁₂ Deficiency: Recognition and Management. *Am Fam Physician*. 2017;96(6):384–389.

Question 33

A 31-year-old man with a 15-year history of ileocolonic Crohn's disease comes in for a follow-up visit 3 months after he underwent resection of 100 cm of his distal ileum for several fibrotic strictures. Since surgery, he has been receiving subcutaneous ustekinumab 90 mg every 8 weeks for post-operative recurrence prevention. Clinically he is doing better with a decrease in his abdominal pain and nausea, but he continues to have diarrhea along with gas and bloating. On physical examination, he has a midline abdominal incisional scar that has healed well, and his abdomen is nontender to palpation but mildly tympanic to percussion. A restaging colonoscopy and computed tomography enterography are both done without any evidence of active inflammation. As part of his healthcare maintenance, you order a dual-energy x-ray absorptiometry bone density scan, arrange for skin cancer screening, and obtain nutritional laboratory tests.

Which nutrient deficiency is most likely to be found and why?

- A. Vitamin A due to exocrine pancreas insufficiency
- B. Vitamin C due to inadequate oral intake
- C. Folate due to small intestinal bacterial overgrowth
- D. Vitamin B₁₂ due to malabsorption from his ileal resection
- E. Vitamin D deficiency due to fat malabsorption

CORRECT ANSWER: E

RATIONALE

The ileum absorbs both vitamin B₁₂ and bile salts. If more than 60 cm of ileum is resected, vitamin B₁₂ deficiency is likely to occur; however, there is enough vitamin B₁₂ stored in the body that deficiency typically takes several years to occur. His surgery was only 3 months before this visit. However, when 100 cm or more of ileum has been resected, the increased hepatic synthesis of bile salts is not enough to keep up with the stool losses and a degree of fat malabsorption occurs. Since vitamin D is fat-soluble, he would have developed a vitamin D deficiency as a result. Although exocrine pancreas insufficiency also leads to the malabsorption of fat-soluble vitamins, he does not have any risk factors for this, nor does he have any symptoms or signs of vitamin A deficiency. Vitamin C deficiency due to inadequate oral intake is rare and symptoms of this deficiency include poor wound healing, which he does not have. Although he is at high risk for small intestinal bacteria overgrowth due to his resection,

vitamin B₁₂ deficiency occurs as a result of this, not folate deficiency.

REFERENCE
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Question 34

A 21-year-old man who relocated here from India comes into your office with abdominal cramping, diarrhea, and abdominal bloating going on for the past 3 months. He has developed swelling in his ankles and weight loss as a result. His primary care physician provided laboratory test results that are shown below.

His primary care physician also submitted several stool and serological studies looking for *Giardia lamblia*, *Cryptosporidium parvum*, *Strongyloides stercoralis*, and *Entamoeba histolytica*, which were all negative. You perform an esophagogastroduodenoscopy, which shows moderate villous blunting with an increase in intraepithelial lymphocytes, but periodic acid-Schiff staining is negative. Gastric mucosa shows mild chronic gastritis but is negative for *Helicobacter pylori* organisms.

What is the next best treatment for this patient and why?

- A. Doxycycline 100 mg twice daily for 3 months for tropical sprue

Laboratory Test	Result	Reference Range
Anti-tissue transglutaminase IgA, U/mL	1	0-15
Folate, serum, ng/mL	1.2	1.8-9.0
Hemoglobin, blood, g/dL	9.2	14-18
IgA, mg/dL	200	90-325
Mean corpuscular volume, fL	110	80-98
Vitamin B ₁₂ , serum, pg/mL	232	200-800

- B. Budesonide 9 mg daily for 1 month for refractory celiac sprue
- C. Rifaximin 550 mg three times daily for 2 weeks for small intestinal bacteria overgrowth
- D. Ceftriaxone 2 g intravenously once daily for 2 weeks for Whipple's disease
- E. Intravenous immune globulin therapy for common variable immunodeficiency

CORRECT ANSWER: A

RATIONALE

Tropical sprue is a chronic diarrheal disease, possibly of infectious origin, that involves the small intestine and results in diarrhea, malabsorption, and weight loss. Tropical sprue occurs primarily in South Asia and in the Caribbean, resulting in a megaloblastic anemia due to folate deficiency. If stool and serology tests have excluded other causes, esophagogastroduodenoscopy with duodenal biopsies will show features that closely mimic celiac sprue; however, celiac serologies will be negative. Treatment is with a tetracycline antibiotic, which completely reverses the intestinal and hematologic abnormalities of tropical sprue in most patients. Although small intestinal bacteria overgrowth can cause similar symptoms, folate levels tend to be elevated since bacteria synthesize folic acid. Whipple's disease is caused by *Tropheryma whipplei* infection and although it causes diarrhea, malabsorption, and weight loss, it is also commonly associated with neurologic or psychiatric symptoms, and duodenal biopsies have nonacid-fast granules in macrophages that stain positive for periodic acid-Schiff, which is not the case here. Lastly, common variable immunodeficiency would be unlikely given the normal IgA level and lack of history of recurrent infections.

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Wanke CA. Tropical Sprue: Enteropathy. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 2015;1297-1301. doi:10.1016/B978-1-4557-4801-3.00104-1

Question 35

A 62-year-old man with a history of heavy alcohol abuse and acute recurrent pancreatitis is admitted to the hospital after presenting with acute epigastric abdominal pain. He is found to have lipase levels of 2218 U/L (reference range, 10-140 U/L), and a computed tomography scan of the abdomen with intravenous contrast shows peripancreatic fat stranding as well as calcifications and pancreas duct dilation in the body of the pancreas. On review of systems, he reports that he has been having worsening diarrhea at home that is foul smelling and hard to flush and that it can occur in the middle of the night. When he uses the bathroom in the middle of the night, he is having difficulty walking to the bathroom, which has resulted in several falls and bruises, which are taking longer to heal than usual. His body mass index is 17 kg/m² and on examination, he appears cachectic with temporal wasting. His sclerae are anicteric, but he does have gray plaques on his conjunctivae. His abdomen is slightly protuberant and tender to palpation in the epigastrium. He also has several red-brown follicular papules on his elbows and knees. He is currently on a clear liquid diet as well as receiving intravenous lactated ringers.

Which of the following vitamin deficiencies is this patient suffering from?

- A. Vitamin B₁₂
- B. Vitamin C
- C. Vitamin A
- D. Vitamin B₁
- E. Vitamin B₃

CORRECT ANSWER: C

Laboratory Test	Result	Reference Range
5-Hydroxyindoleacetic acid, urine, mg/24 hours	300	2-9
Alkaline phosphatase, serum, U/L	421	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	145	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	125	10-40
Bilirubin (total), serum, mg/dL	2.6	0.3-1.0
Chromogranin A, serum, ng/mL	>1200	<93

RATIONALE

This man is suffering from steatorrhea due to fat malabsorption as a result of diminished lipase production and secretion by the pancreas. This is a consequence of any disease that chronically injures the pancreas or obstructs the pancreatic duct. In this case, repeated episodes of alcohol-induced pancreatitis have led to chronic damage to the acinar cells that are responsible for exocrine function. In addition to fat malabsorption, malabsorption of the fat-soluble vitamins A, D, E, and K take place. Vitamin A deficiency causes night blindness; on physical examination, gray conjunctival plaques called Bitot’s spots and a follicular hyperkeratosis, all of which this patient is suffering from. Vitamin B₁ (thiamine), vitamin B₃ (niacin), vitamin B₁₂ (cobalamin), and vitamin C are all water soluble and do not rely on exocrine pancreas function to be absorbed. Although symptoms of difficulty walking and easy bruising can result from these vitamin deficiencies, in this case, vitamin E and vitamin K deficiencies are the more likely explanation given his exocrine pancreas insufficiency.

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Debelo H, Novotny JA, Ferruzzi MG. Vitamin A. *Adv Nutr*. 2017;8(6):992-994. Published 2017 Nov 15. doi:10.3945/an.116.014720

Question 36

A 64-year-old woman presents to your office for

progressive diarrhea and abdominal pain over the last 9 months. These symptoms have also been associated with occasional flushing episodes as well as forgetfulness and weight loss. On physical examination, she has facial flushing and erythematous, with excoriated skin around her neck. Laboratory analysis reveals a normal complete blood count, but her liver function tests show the following results listed above.

A colonoscopy was performed, which was normal; however, a computed tomography of her abdomen revealed a tumor in the distal ileum with infiltration into the mesentery and numerous liver lesions consistent with metastases.

Which nutrient deficiency is contributing to her symptoms?

- A. Thiamine
- B. Niacin
- C. Zinc
- D. Iodine
- E. Biotin

CORRECT ANSWER: B

RATIONALE

This patient has carcinoid syndrome given the laboratory and imaging findings. In carcinoid syndrome, tumor cells suppress endogenous niacin production by diverting tryptophan metabolism toward serotonin and away from niacin. Anorexia and diarrhea, frequently present in carcinoid syndrome, further reduce the availability of exogenous niacin by decreasing the amount ingested and absorbed. The decreased availability of endogenous and exogenous niacin is responsi-

ble for the development of pellagra. Pellagra is the name of the disease caused by niacin (vitamin B₃) deficiency; when severe, it presents with dementia, dermatitis, and diarrhea. Some develop a rash around the neck known as a Casal necklace. Although thiamine, zinc, and biotin deficiencies can cause both dementia and dermatitis, none cause the distinct rash that is seen with niacin deficiency nor are they associated with carcinoid syndrome. Iodine deficiency is linked to hypothyroidism.

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Question 37

A 24-year-old woman is referred to your office for persistent iron deficiency anemia. She has had a low hemoglobin since she started college, but this has been attributed to heavy menstrual bleeding. She has a body mass index of 18 kg/m², and her vital signs are normal. On physical examination, she appears well but with mild conjunctival pallor. Her abdomen is soft to palpation but mildly tympanic to percussion. Her laboratory results show the following below.

Her vitamin B₁₂ and folate are both normal. A pelvic ultrasound showed a heterogeneous uterus with no evidence of fibroid lesions. She has been on oral contraceptive pills for the last several months, and her menorrhagia has resolved.

What is the next best step in determining the cause of her anemia?

- A. Order a magnetic resonance enterography to evaluate for small bowel Crohn's disease
- B. Refer to hematology for hemoglobin electrophoresis testing
- C. Do a fecal immunochemical test to confirm the presence of occult blood in the stool
- D. Perform an esophagogastroduodenoscopy with duodenal biopsies
- E. Check a haptoglobin, lactate dehydrogenase, and indirect bilirubin to evaluate for hemolysis

CORRECT ANSWER: D

RATIONALE

Iron deficiency anemia in a young woman is often due to menstrual bleeding, overt gastrointestinal bleeding, or malabsorption. Inadequate dietary intake is almost never the case in this country. Although she has complained of heavy bleeding in the past, her uterus is normal and combination estrogen and progesterone has decreased the amount of bleeding she has been having. Adults presenting with iron deficiency anemia have occult celiac sprue up to 9 percent of the time, and iron deficiency anemia can be found in up to 46 percent of patients with subclinical celiac sprue. Therefore, an esophagogastroduodenoscopy with duodenal biopsies would be the next best step. Crohn's disease of the small intestine would generally cause abdominal pain and diarrhea if it has also caused significant iron deficiency and a hemoglobinopathy such as sickle cell disease or a thalassemia would have been present earlier than college. Although she could be having an occult bleed from her gastrointestinal tract, this test is best used to screen for colon cancer instead of to

Laboratory Test	Result	Reference Range
Ferritin, serum, ng/mL	4	24-307
Hemoglobin, blood, g/dL	8.9	12-16
Iron, serum, µg/dL	25	50-150
Mean corpuscular volume, fL	72	80-98

determine the etiology of iron deficiency. Lastly, hemolysis would not cause iron deficiency nor microcytosis.

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Question 38

A 37-year-old man comes into the emergency department with acute epigastric pain that started 4 hours prior and is associated with nausea and vomiting. Laboratory values show the following:

A computed tomography of his abdomen shows a heterogeneous appearance of the pancreas with peripancreatic fat stranding consistent with acute pancreatitis but is otherwise normal. He admits to drinking 6 to 8 beers a day, but this is the first time he has ever developed this type of pain. He is admitted to the hospital and started on intravenous lactated ringers and analgesia overnight.

Currently his vital signs are normal, and his examination is only notable for mild tenderness to palpation over his epigastrium. He is asking when he can eat something.

What is the best way to begin nutrition in this patient?

- A. Start with a clear liquid diet for 2-3 days; if tolerated, advance to full liquids
- B. Place a nasojejunal tube and begin continuous tube feeds
- C. Immediately place him on a low-fat diet to include solid foods, and monitor his response
- D. Keep him on intravenous fluids with dextrose until his abdominal pain resolves
- E. Initiate total parenteral nutrition

CORRECT ANSWER: C

RATIONALE

The time to reinstitute oral feedings depends on the severity of the pancreatitis. Given he is not hemoconcentrated as evidenced by a normal hematocrit and BUN and he has no signs of organ failure, his pancreatitis would be characterized as mild. In the absence of an ileus or nausea and vomiting, oral feeding with a low-fat solid diet can be started early (within 24 hours of presentation) as tolerated. Abdominal pain, the serum lipase, or the computed tomography findings do not have to resolve before starting solid foods. Traditionally, clear liquids were always started first and only advanced as tolerated; however, there is no data to support this. If he tried and failed oral feeding due to persistent pain or vomiting or had more severe disease as evidenced by a gastric outlet obstruction or pancreatic necrosis on computed tomography, then enteral feeding with a nasojejunal tube would be best. Total parenteral nutrition is reserved for those who are critically ill and do

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	19	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	21	10-40
Bilirubin (total), serum, mg/dL	0.8	0.3-1.0
Blood urea nitrogen (BUN), serum or plasma, mg/dL	8	8-20
Calcium, serum, mg/dL	9.2	8.6-10.2
Hematocrit, blood, %	40	42-50
Lipase, serum, U/L	621	10-140

not tolerate enteral feeding at all. Enteral feeding should even be attempted first in these patients as it leads to better outcomes in part due to its ability to maintain the intestinal barrier and prevent bacterial translocation from the gut.

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Tenner S, Baillie J, DeWitt J, Vege SS; American College of Gastroenterology. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol.* 2013;108(9):1400-1416. doi:10.1038/ajg.2013.218

Question 39

A 52-year-old woman with diabetic gastroparesis comes to see you for a 6-month follow-up visit. She has poorly controlled type 2 diabetes mellitus with a hemoglobin A1C of 11.5% and was first diagnosed with gastroparesis 3 years ago as evidenced by solid gastric emptying of 15% at the 4-hour mark on a scintigraphy study. Her symptoms previously were well managed with ondansetron as needed and periodic uses of either metoclopramide or erythromycin. However, over the last several months, she cannot find any relief and continues to vomit after drinking or eating anything. Her body mass index is down to 16 kg/m², and she has evidence of decreased skin turgor and muscle wasting on physical examination.

Laboratory analysis shows the following:

You decide to have her admitted to the hospital for intravenous fluids where you obtain a computed tomography and perform an esophagogastroduodenoscopy (EGD). She does not have any evidence of a mechanical gastric outlet obstruction, only an enlarged stomach with a large amount of retained food with no visible antral contractions.

What is the next best step in managing her gastroparesis?

- A. Place a percutaneous gastrojejunal tube for post-pyloric tube feeding and gastric venting
- B. Start her on oral domperidone 10 mg three times daily before meals
- C. Consult a surgeon to evaluate her for a laparoscopic pyloromyotomy
- D. Repeat the EGD and inject botulinum toxin into her pyloric sphincter
- E. Refer her to endocrinology to explore using the glucagon-like peptide-1 agonist liraglutide for better glucose control

CORRECT ANSWER: A

RATIONALE

This patient has developed refractory symptoms despite anti-emetics and prokinetics and is clearly in need of nutritional support. This is evidenced by her low body mass index and physical examination findings of muscle atrophy and dehydration. Of these options, the only one that will provide long-term nutritional support is the placement of an enteric feeding tube. The benefit to placing a gastrostomy tube in addition to the jejunal feeding tube is to allow for venting of the stomach, which results in less vomiting and reduces the need of a hospitalization for any acute worsening of symptoms. Domperidone works very similarly to metoclopramide but is a peripheral dopamine

Laboratory Test	Result	Reference Range
Creatinine, serum, mg/dL	1.6	0.7-1.5
Potassium, serum, mEq/L	2.5	3.5-5.0
Sodium, serum, mEq/L	132	136-145

antagonist, which does not cross the blood-brain barrier. However, given she has already failed oral therapy, this is not as likely to succeed. Although a pyloromyotomy has shown benefit at 3 months in small trials, long-term studies are needed before this can be routinely recommended. Randomized controlled trials have failed to show any improvement in symptoms with the use of intrapyloric botulinum toxin injection. Lastly, liraglutide is contraindicated in patients with gastroparesis, as glucagon-like peptide 1 receptor agonists delay gastric emptying.

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diabetic gastroparesis: efficacy, tolerability, and quality-of-life outcomes in a multicenter controlled trial. DOM-USA-5 Study Group. *Clin Ther.* 1998;20(3):438-453. doi:10.1016/s0149-2918(98)80054-4

Question 40

A 28-year-old woman is referred to you by her bariatric surgeon for anemia. She has a history of morbid obesity (body mass index 44 kg/m²) complicated by obstructive sleep apnea and underwent a laparoscopic Roux-en-Y gastric bypass surgery 2 years ago. Since then, she has lost over 150 pounds but developed fatigue and malaise, prompting her surgeon to obtain further testing. Laboratory values show the following below.

Fecal immunochemical testing was done and is negative for occult blood. You inquire further about her diet and vitamin use, and she has been eating a vegetarian diet to help maintain her weight and has been compliant with the daily over-the-counter multivitamin her surgeon prescribed after surgery.

- Which of the following most likely explains her iron deficiency?
- A. Small intestinal bacteria overgrowth (SIBO) because of her bypass surgery
 - B. A bleeding marginal ulcer at her gastrojejunal anastomosis
 - C. Vitamin C (ascorbic acid) malabsorption given duodenal bypass
 - D. She is not getting the required iron she needs in her multivitamin
 - E. Her diet is resulting in inadequate amounts of iron intake

Laboratory Test	Result	Reference Range
Ferritin, serum, ng/mL	8	24-307
Folate, serum, ng/mL	>20	1.8-9.0
Hemoglobin, blood, g/dL	9.8	12-16
Mean corpuscular volume, fL	82	80-98
Vitamin B ₁₂ , serum, pg/mL	343	200-800

CORRECT ANSWER: D**RATIONALE**

Iron deficiency is one of the most common nutrient deficiencies after bariatric surgery and is largely the result of bypassing the duodenum and proximal jejunum where iron is absorbed. In addition to this malabsorption, a decrease in acid production in the gastric remnant can be further responsible. Therefore, iron supplementation is necessary to avoid deficiency and subsequent anemia as this patient has developed. Although intravenous iron may be superior to oral iron in terms of tolerance, oral iron in the amounts of 150 to 300 mg, 2 to 3 times daily, is typically sufficient after a gastric bypass surgery. However, over-the-counter multivitamins do not contain this required amount and is the most likely reason for her deficiency. Although iron intake from meat (heme iron) is better absorbed than nonheme iron found in vegetables, her iron status is not dependent on her diet given her duodenum has been bypassed. Since iron needs to be conjugated to vitamin C in order to remain in an absorbable form, iron deficiency can occur in vitamin C deficiency. However, vitamin C deficiency is not a complication of bariatric surgery, and she presumably is getting adequate intake of vitamin C in her diet. Although bleeding anastomotic ulcers and SIBO are complications of bariatric surgery, her fecal immunochemical test was negative for any occult blood and SIBO does not cause iron deficiency.

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Question 41

A 29-year-old man comes into your office with difficulty swallowing for the last year. He does have a history of eczema and exercised-induced asthma but is not on any medications for these. An esophagogastroduodenoscopy (EGD) with biopsies in the proximal and distal esophagus reveals eosinophilic esophagitis and you start him on esomeprazole 40 mg twice daily for 2 months. You perform a repeat EGD in 2 months to assess his response to therapy and find that he continues to have more than 25 eosinophils per high-power field throughout his esophagus. You plan to start twice-daily swallowed budesonide, but he asks whether there is any diet he can do to help with this instead.

Which 2-food elimination diet is the most likely to succeed in this patient?

- A. Nuts and eggs
- B. Seafood and soy
- C. Dairy and wheat
- D. Soy and nuts
- E. Dairy and eggs

CORRECT ANSWER: C**RATIONALE**

Eosinophilic esophagitis is a chronic, immune-mediated esophageal disease triggered predominantly by food antigens. However, this condition does not rely on IgE-mediated mechanisms and as a result, available food allergy tests are suboptimal to predict food triggers for eosinophilic esophagitis, especially in adults. Traditionally an empiric 6-food elimination diet has been used to try and identify the culprit food group; however, adher-

ence to the elimination of multiple food groups can be difficult. Thus, a 4-food elimination diet or sequentially increasing the number of eliminated foods is becoming more common. It is known that 90 percent of responders to 4-food elimination diets only had 1 or 2 causative food groups. The 2 most common agents responsible for reactions in eosinophilic esophagitis are cow's milk and wheat; therefore, C is the correct answer here. Eggs are the third most responsible agent. Multiple studies have consistently shown that nuts and fish/seafood rarely trigger eosinophilic esophagitis.

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Question 42

A 35-year-old woman is referred to you by her dentist for concerns of acid reflux. She reports that at her regular cleaning, the dentist commented on the amount of enamel erosion she had and is concerned she could be suffering from silent gastroesophageal reflux disease. When talking with her, she denies any heartburn, chest discomfort or any other red flags such as difficulty swallowing, melena, dyspepsia, or unexplained weight loss. Her body mass index is 31 kg/m² and on physical examination, the only notable finding are scars on the dorsum of her right hand. You start her on a once-daily proton pump inhibitor (PPI) before breakfast and see her back in follow-up 1 month later. At her follow-up visit, she reports she thinks the omeprazole is making her nauseous. You decide to proceed with an esophagogastroduodenoscopy to evaluate her symptoms further.

Which of the following findings are you most likely to see on her endoscopy?

- A. A clean-based ulcer in the gastric antrum
- B. Numerous fundic gland polyps in the gastric body

- C. Villous blunting in the duodenal bulb
- D. White mucosal plaque-like lesions in the proximal esophagus
- E. Several Mallory-Weiss tears in the distal esophagus

CORRECT ANSWER: E

RATIONALE

This patient has several warning signs of bulimia nervosa including the enamel destruction and the calluses on her hand. Calluses on the dorsum of the hand (Russell's sign) are nearly pathognomonic, due to pressure of the teeth against the skin while stimulating the gag reflex to induce vomiting. Forceful vomiting can cause longitudinal mucosal lacerations (Mallory-Weiss tears) in the distal esophagus and proximal stomach. Peptic ulcer disease is most commonly caused by *Helicobacter pylori* infection and nonsteroidal antiinflammatory drugs; additionally, she denies symptoms of dyspepsia that can often be experienced in the setting of a gastric ulcer. Fundic gland polyps can occur after long-term PPI use (one study observed them after a mean treatment duration of 32.5 months); however, this patient has only been on a PPIs for 1 month. Villous blunting is seen in cases of enteropathy with celiac sprue being one of the more common causes and would not explain the overall picture in this case. Lastly, white mucosal plaques consistent with Candida esophagitis are unlikely given her lack of dysphagia and the risk of this infection is increased in those who are immunosuppressed, not who have recurrent vomiting.

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Question 43

An 18-year-old man born with VACTERL (vertebral, anal atresia, cardiac, trachea, esophageal, renal, and limb defects) syndrome complicated by right ventricular and tricuspid valve hypoplasia and esophageal atresia is transitioning to your care from his pediatric gastroenterologist now that he is an adult. He underwent a Fontan procedure to decrease the workload of his functionally single ventricle and has been getting continuous tube feeds via a gastrojejunostomy tube his whole life. He reports abdominal cramping throughout the day and has 4 to 5 episodes of diarrhea daily as well. He also notices that his abdomen and extremities get swollen. On physical examination, his weight is 47.7 kg, height is 158.2 cm, heart rate is 56 bpm, and oxygen saturation is 87% on room air. His heart is notable for a murmur; however, his lungs are clear to auscultation. His abdomen is distended but soft and his percutaneous enteric feeding tube site is without erythema. A complete metabolic profile reveals normal electrolytes and liver enzymes, but a serum albumin of 2.1 g/dL (reference range, 3.5-5.5 g/dL). A complete blood count is normal except for a low mean corpuscular volume of 79 fL (reference range, 80-98 fL). Your next step is to order stool studies.

Which stool test result will most likely explain the cause of his diarrhea?

- A. Fecal calprotectin
- B. Fecal electrolytes and osmolality
- C. Fecal bile acids
- D. Fecal alpha-1 antitrypsin
- E. Fecal elastase

CORRECT ANSWER: D

RATIONALE

This patient has protein-losing enteropathy (PLE) due to the cardiac surgery he underwent for his congenital heart defect. The precise pathophysiology in this circumstance remains unknown, but this surgery causes an increase in central venous pressures, resulting in intestinal lymphatic con-

gestion and enterocyte dysfunction. This can lead to the development of PLE weeks to years later. His diarrhea is a result of this, and proper testing includes the measurement of alpha-1 antitrypsin losses in the stool. This is the test of choice to detect a protein leak in the intestinal mucosa, as it is usually excreted in only small quantities in the stool and is not metabolized by other organs. Fecal calprotectin is elevated in cases of inflammation and although inflammatory bowel disease can cause a PLE, there is no reason to suspect this diagnosis in this patient. Fecal electrolyte and osmolality testing is useful in differentiating whether diarrhea is due to osmotic or secretory causes but not in determining protein loss. Bile acid testing can determine if bile malabsorption is to blame, and elastase is more useful in evaluating for pancreatic exocrine insufficiency.

REFERENCE

Johnson JN, Driscoll DJ, O'Leary PW. Protein-losing enteropathy and the Fontan operation. *Nutr Clin Pract*. 2012;27(3):375-384. doi:10.1177/0884533612444532

Question 44

A 14-year-old boy presents with chronic diarrhea and progressive symptoms of lower extremity edema, easy bruising, and inability to gain weight over the past year. Laboratory tests reveal a vitamin D deficiency, elevated prothrombin time/international normalized ratio, and hypoalbuminemia. His liver function tests are normal. Stool alpha-1-antitrypsin is markedly elevated. An abdominal ultrasound reveals a normal liver. Esophagogastroduodenoscopy reveals a normal esophagus and stomach, with extensive scattered white spots over the duodenal mucosa. Duodenal biopsies reveal markedly dilated lymphatics that are most apparent in the tips of the villi. In addition to a high protein diet, which of the following should also be increased in the diet?

- A. Fiber and roughage
- B. Long-chain fatty acids

- C. Medium-chain fatty acids
- D. Complex carbohydrates
- E. Short-chain fatty acids

CORRECT ANSWER: C

RATIONALE

This patient is presenting with a protein-losing enteropathy, likely related to primary intestinal lymphangiectasia, as evidenced by elevated protein levels in the stool and fat-soluble vitamin deficiencies, as well as lymphangiectasias on endoscopy. One way to reduce lymphatic flow and subsequent enteric lymph leakage and protein loss is to be on a low-fat diet. This includes a diet low in long-chain fatty acids. However, to get adequate calories, fat should be consumed in the form of medium-chain fatty acids as these are absorbed directly into the portal circulation, rather than the lymphatic circulation. Short-chain fatty acids are byproducts of bacteria fermentation in the colon and supply energy to colonocytes but do not have nutritional value. High fiber and complex carbohydrate diets are better suited for dumping syndrome.

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Question 45

A 52-year-old man with a history of gastroesophageal reflux disease comes to see you for the recent development of nausea and vomiting. He underwent a Nissen fundoplication and hiatal hernia repair 6 months ago to better control his acid reflux and get him off proton pump inhibitor therapy. Although he reports his heartburn is under better

control, he has noticed that over the last several weeks he vomits in the mornings. Most often it is undigested food that is consistent with his dinner from the night before. He may vomit sometimes during the day as well, especially after larger meals. When this occurs, it is associated with nausea and abdominal pain. On physical examination, his abdomen is soft, nontender, and nondistended with normoactive bowel sounds. You obtain a plain abdominal radiograph, which shows a normal bowel gas pattern and normal colonic stool burden. You recommend he try eating smaller meals more frequently that are low in fat and residue.

Why will minimizing his fat intake help his symptoms?

- A. Fat decreases the lower esophageal sphincter tone, allowing for easier regurgitation
- B. Fat increases tonic and phasic pyloric pressures, resulting in nausea and vomiting
- C. Fat increases ghrelin secretion, resulting in decreased appetite and vomiting
- D. Fat increases the gastrocolic reflex, leading to nausea and abdominal cramping
- E. Fat increases gallbladder emptying, leading to bile reflux and epigastric pain

CORRECT ANSWER: B

RATIONALE

This patient is demonstrating symptoms of delayed gastric emptying, which can occur after anti-reflux surgeries. The underlying mechanisms by which fat further causes delayed gastric emptying is by relaxing the proximal stomach, decreasing antral and duodenal contractility and increasing tonic and phasic pyloric pressures. In addition, fat decreases ghrelin, which results in a decrease in appetite. Although fat does increase gallbladder emptying and the gastrocolic reflex, symptoms of these are not in line with gastroparesis and what this patient is experiencing. Rather, patients may have right upper quadrant pain and diarrhea as the predominant symptoms. Lastly, fat intake has no direct influence over the lower esophageal sphincter.

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Question 46

An 82-year-old man has been complaining of progressively worsening dysphagia over the last 6 months with a 30-pound weight loss. You perform an esophagogastroduodenoscopy, which reveals a near-obstructing mass in the lower third of the esophagus with biopsies confirming the diagnosis of adenocarcinoma. A computed tomography of the chest, abdomen, and pelvis is then performed showing metastases to the liver and lungs, and chemotherapy and radiation therapy are started. To receive nutrition, you place a gastrostomy tube to begin tube feeding. He is seen by a registered dietitian who recommends bolus feeding, 250 mL 5 times daily to provide 2500 kcal and 120 g of protein. He begins tube feeds but feels nauseous and bloated after each feed. It has been 4 hours since his last feed and you determine 500 mL of formula remain in the stomach.

Which of the following would be the next best step to improve his tolerance to tube feeds?

- A. Switch to continuous tube feeds at a rate of 30 mL per hour
- B. Change his tube feeds to a lactose-free formula
- C. Administer liquid metoclopramide 10 mg before feeds

- D. Change the formula to one that is more calorie rich
- E. Increase the amount of time between bolus feeds

CORRECT ANSWER: C

RATIONALE

Enteral tube feeding intolerance is a common occurrence during total enteral feeding. Although the causes behind this are not fully understood, it is felt that factors affecting gastrointestinal motility are the most likely to be responsible. In this case, his gastric residual volume is over 500 mL, which is a sign of poor gastric emptying. Although switching him to a continuous rate of tube feeds or increasing the amount of time between boluses can assist in emptying, neither will meet his nutritional needs. Although changing to a calorie-dense formula will lower the total volume administered, it will not be by a significant enough amount to prevent a continued high residual. Therefore, pharmacologic intervention is the best option. Although lactose intolerance is common in the elderly, most standard formulas are lactose-free already.

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Question 47

A 19-year-old woman is admitted to the hospital after presenting to the emergency department with progressive nausea and vomiting. She was found to have numerous laboratory abnormalities which are shown at the top of the following page.

You are consulted to see her and note in the chart that her body mass index is 13.8 kg/m² with a

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	1.9	3.5-5.5
Aminotransferase, serum alanine (ALT, SGPT), U/L	100	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	200	10-40
Creatinine, serum, mg/dL	1.7	0.7-1.5
Lipase, serum, U/L	95	10-140
Potassium, serum, mEq/L	2.3	3.5-5.0
Sodium, serum, mEq/L	124	136-145

height of 170.2 cm and body weight of 40 kg. On physical examination, she is severely cachectic, appearing with diffuse muscle atrophy. Her abdomen is scaphoid with minimal tenderness to palpation and hypoactive bowel sounds. You conduct a SCOFF (sick, control, one, fat, food) screening test, and she answered yes to 3 of the questions, strongly indicating the presence of an underlying eating disorder. Psychiatry is consulted as well but will not transfer her to an eating disorder unit until her nausea and vomiting have resolved. An esophagogastroduodenoscopy and gastric emptying scintigraphy studies are performed and are normal. A nasogastric tube is placed to begin enteral feeding, and she continues to vomit.

Which of the following is the next best study in determining the cause of her vomiting?

- A. Computed tomography of the head
- B. Magnetic resonance cholangiopancreatography
- C. Video capsule endoscopy
- D. Magnetic resonance arteriogram of the abdomen
- E. 24-hour pH/impedance test

CORRECT ANSWER: D

RATIONALE

This patient is most likely suffering from anorexia nervosa as evidenced by her abnormal response to the SCOFF questionnaire. Patients with this disorder can develop numerous complications, including gastroparesis, elevated liver function tests, acute pancreatitis, and dysphagia. Although she has symptoms of gastroparesis, her empty-

ing study was normal, which may indicate there is postpyloric dysfunction. Another complication of anorexia nervosa is superior mesenteric artery (SMA) syndrome, which occurs primarily in settings of profound weight loss. SMA syndrome occurs because of mesenteric fat loss leading to narrowing of the space between the SMA and aorta, which results in compression of the third portion of the duodenum. This would explain why her stomach and proximal duodenum appeared normal on esophagogastroduodenoscopy. The best test to diagnose this is an angiogram or arteriography study, as the angle and space between the vessels can be measured and provide additional details such as the amount of intraabdominal fat that is present. Computed tomography of the head is sometimes done to evaluate for nausea and vomiting, but usually when there are concomitant neurologic symptoms and/or a gastrointestinal source has been excluded. There is no reason to suspect a pancreatobiliary abnormality; thus, a magnetic resonance cholangiopancreatography would not be useful. Video capsule endoscopy is not used in the workup of nausea and vomiting. A 24-hour pH/impedance test is used to evaluate refractory reflux symptoms, and although gastroesophageal reflux disease is a common cause of nausea and vomiting, a more likely explanation in the setting of anorexia and cachexia is SMA syndrome.

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Laboratory Test	Result	Reference Range
Folate, serum, ng/mL	6	1.8–9.0
Hemoglobin, blood, g/dL	14.2	12–16
Mean corpuscular volume, fL	82	80–98
Tissue transglutaminase antibody, IgA, U/mL	2	<4.0
Vitamin B ₁₂ , serum, pg/mL	112	200–800

Question 48

A 44-year-old woman with a 20-year history of ileal Crohn's disease comes in for a follow-up visit. She underwent an ileocolic resection due to a fibrotic stricture of her ileocecal valve 1 year ago. Since her surgery, she has been on no medical therapy for her Crohn's disease but does take occasional antacids for heartburn. Although she is no longer having abdominal pain and constipation, she has developed diarrhea as well as gas and bloating. As a result, she has not been eating as much as she used to. You check blood and stool tests, and you see that both her C-reactive protein and fecal calprotectin are normal. You also check a 7-alpha-hydroxy-4-cholesten-3-one (7 alpha C4) test, and hers is 75 ng/mL (reference range, <62 ng/mL). Additional laboratory tests show the following above.

You set her up for an esophagogastroduodenoscopy and ileocolonoscopy, which shows mild chronic gastritis but an otherwise healthy-appearing ileocolic anastomosis without any aphthous ulcers. What is the most likely reason for her vitamin B₁₂ deficiency?

- A. Small intestinal bacteria overgrowth
- B. Autoimmune gastritis
- C. Frequent antacid use
- D. Malabsorption due to ileal resection
- E. Inadequate dietary intake

CORRECT ANSWER: D

RATIONALE

Vitamin B₁₂ is absorbed in the terminal ileum, and deficiency can occur when the distal 60 cm of ileum is resected. The fact that her 7 alpha C4 level is elevated indicates she is also malabsorbing bile salts, which confirms she is having malabsorption at the site of her distal ileum. Although she is at risk for small intestinal bacterial overgrowth (SIBO), due to the loss of her ileocecal valve, folate levels tend to be elevated as folic acid is a byproduct of bacteria fermentation in SIBO, and hers is normal. Autoimmune gastritis is seen in cases of pernicious anemia but her hemoglobin and MCV are both normal. Acid suppressants can also lead to vitamin B₁₂ deficiency, but this is usually seen in chronic proton pump inhibitor usage and not occasional antacid use. Vitamin B₁₂ deficiency due to poor dietary intake is also rare in this country, but if seen is typically in those who are strict vegans.

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Langan RC, Goodbred AJ. Vitamin B12 Deficiency: Recognition and Management. *Am Fam Physician*. 2017;96(6):384-389.

Question 49

A 56-year-old man presents to the emergency department with worsening right upper quadrant pain, nausea with vomiting, and weakness. He is confused, with tremors, and he is visibly jaundiced. His wife reports that he continues to drink a pint of vodka daily. Laboratory values below.

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	155	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	312	10–40
Bilirubin (total), serum, mg/dL	22.1	0.3–1.0

He is admitted to the hospitalist service, placed on a CIWA (Clinical Institute Withdrawal Assessment for Alcohol) protocol, and you are consulted to see him. On physical examination, he is drowsy and will only open his eyes to loud stimuli. He is not oriented to person, time, or place. He has diffuse muscle wasting, is visibly jaundiced, and has a protuberant abdomen without a positive fluid wave. Deep tendon reflexes are normal. After receiving a nasogastric tube, lactulose is administered along with rifaximin for presumed hepatic encephalopathy. A diagnostic paracentesis is performed and is negative for peritonitis. The remainder of his infectious workup is negative as well. He has been having 5 bowel movements daily but remains confused.

Which of the following supplements will help improve his mental status?

- A. Oral zinc 250 mg three times daily.
- B. Intravenous folic acid 1 mg once daily.
- C. Intravenous multivitamin once daily.
- D. Oral thiamine 100 mg once daily.
- E. Intravenous thiamine 500 mg 3 times daily.

CORRECT ANSWER: E

RATIONALE
Wernicke’s encephalopathy is associated with chronic alcohol use and is due to thiamine deficiency from poor dietary intake, reduced absorption, and decreased hepatic storage. Disorientation and confusion are symptoms of this condition, which can worsen if intravenous glucose is administered before giving thiamine. Thiamine should be administered intravenously as oral absorption can be suboptimal in those who misuse alcohol. Additionally, the amount of thiamine needed to reverse the neurologic symp-

toms of Wernicke’s encephalopathy is not sufficiently obtained in oral dosing. There has been suggestion that oral zinc can help with hepatic encephalopathy, but there is insufficient evidence to support the use of this. The same can be said of intravenous folic acid and multivitamins. These are frequently used in those who misuse alcohol as part of a ‘banana bag,’ but there is insufficient evidence that these are necessary nor helpful in this setting.

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Patel S, Topiwala K, Hudson L. Wernicke’s Encephalopathy. *Cureus*. 2018;10(8):e3187. Published 2018 Aug 22. doi:10.7759/cureus.3187

Riggio O, Ariosto F, Merli M, et al. Short-term oral zinc supplementation does not improve chronic hepatic encephalopathy. Results of a double-blind crossover trial. *Dig Dis Sci*. 1991;36(9):1204-1208. doi:10.1007/BF01307509

Question 50
An 84-year-old woman is admitted to the hospital after presenting with recurrent left lower quadrant abdominal pain. She undergoes a computed tomography of her abdomen and pelvis, which reveals marked thickening of the sigmoid colon, a small adjacent fluid collection, and a colocutaneous fistula. Her medical history is notable for chronic obstructive pulmonary disease, and she is on oxygen at home via a nasal cannula. In addition, she has a history of a cerebral vascular accident on aspirin 81 mg and clopidogrel 75 mg once daily. Laboratory values show the following:

Colorectal surgery recommends medical management given her comorbidities, and gastroenterology is consulted.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	2.9	3.5-5.5
Creatinine, serum, mg/dL	2.0	0.7-1.5
Prealbumin, serum, mg/dL	15	16-30

Which of the following would be the most effective way to manage her nutrition in this setting?

- A. Place a nasojejunal tube and begin enteral feeding and reevaluate in 4 weeks
- B. Complete bowel rest for 3 days with intravenous fluids followed by a clear liquid diet
- C. Total parenteral nutrition for the next 2 weeks then switch to an oral diet
- D. Total parenteral nutrition with repeat imaging in 12 weeks
- E. Start high protein oral supplements 3 times daily alongside her meals

CORRECT ANSWER: E

RATIONALE

Colocutaneous fistulae is a rare complication of diverticulitis occurring in 1% of cases. These usually occur as a result of a perforation or abscess, distal obstruction due to a colonic stenosis or complication of an abscess drainage, or previous bowel resection. However, given this fistula is so distal in the gastrointestinal tract (arising from the sigmoid colon), there is no reason why this patient cannot continue to get full nutrition via an oral route. Since her serum albumin and prealbumin are low, adding high protein supplements would be warranted. If she had an enterocutaneous fistula arising from the proximal gastrointestinal tract, placing a nasoenteric tube distal to the fistula opening can allow enteral feeding to take place. Complete bowel rest coupled with total parenteral nutrition is better suited for enterocutaneous fistulae arising from the small intestine, especially if the output is high (>500 mL daily).

REFERENCE

Dudrick SJ, Maharaj AR, McKelvey AA. Artificial nutritional support in patients with gastrointestinal fistulas. *World J Surg.* 1999;23(6):570-576. doi:10.1007/pl00012349

CHAPTER 2

Acid diseases of the stomach

David Leiman, MD and John Clarke, MD, AGAF

Question 1

A 52-year-old man with chronic dyspepsia is referred for outpatient upper endoscopy. The examination reveals patchy mucosal changes in the gastric body, and biopsies reveal chronic active gastritis with staining positive for *Helicobacter pylori* as well as gastric intestinal metaplasia (GIM) without dysplasia, complete subtype.

What is the most appropriate next step in management of the patient?

- A. Check a stool *H pylori* antigen test
- B. Periodic surveillance for GIM
- C. Proton pump inhibitor therapy
- D. Treatment of *H pylori* with follow-up testing to confirm eradication

CORRECT ANSWER: D**RATIONALE**

H pylori is a carcinogen and accounts for the majority of noncardia gastric cancers worldwide. Although a minority of patients infected with *H pylori* will develop cancer, the infection can progress to cancer through the Correa cascade, with the major driver suspected to be *H pylori* infection. This stepwise progression has several discrete stages, which include normal mucosa, chronic non-atrophic gastritis, chronic atrophic gastritis, GIM, dysplasia, and cancer. As a result, current American Gastroenterological Association guidelines recommend treating *H pylori* and confirming eradication in the context of GIM. Given that the histology reveals stain-

ing positive for *H pylori*, stool antigen testing is unnecessary. Treating with a PPI alone would be incorrect, as *H pylori* must be eradicated. Although surveillance of GIM is appropriate in some circumstances, neglecting to treat *H pylori* would leave this patient with a major risk factor for cancer. Given variable susceptibility, and increasing antibiotic resistance, confirmation of eradication is a necessary component of treatment for *H pylori*.

REFERENCES

Gawron AJ, Shah SC, Altayar O, et al. AGA Technical Review on Gastric Intestinal Metaplasia—Natural History and Clinical Outcomes. *Gastroenterology*. 2020; 158:705-731. <https://doi.org/10.1053/j.gastro.2019.12.001>

Gupta S, Li D, El Serag HB, et al. AGA Clinical Practice Guidelines on Management of Gastric Intestinal Metaplasia. *Gastroenterology*. 2020;3:693-702. <https://doi.org/10.1053/j.gastro.2019.12.003>

Question 2

In a patient with untreated *Helicobacter pylori* found to have nondysplastic gastric intestinal metaplasia (GIM), what is the most appropriate approach for evaluating the associated cancer risk?

- A. Assess the patient's concern about cancer risk to determine whether surveillance or repeat endoscopy in 1 year is appropriate

- B. Repeat endoscopy every 2-3 years to evaluate for any endoscopic lesions
- C. Repeat endoscopy within 1 year to evaluate extent of GIM
- D. No further endoscopy due to low risk of cancer

CORRECT ANSWER: A

RATIONALE

Patients with GIM have an increased risk of non-cardia gastric cancer compared with those who do not have GIM. Among patients with GIM, mostly from outside the United States, the cumulative incidence of gastric cancer at 3 years, 5 years, and 10 years was 0.4%, 1.1%, and 1.6%, respectively. However, these data are based on low or very low quality of evidence. Among patients in the United States, the 5-year cumulative incidence of non-cardia gastric cancer is 0.9%. Acknowledging that some patients may have a higher risk of gastric cancer or put a higher value on a reduction in gastric cancer mortality, it is reasonable to elect for surveillance or repeat endoscopy within 1 year for risk stratification based on shared decision-making with patients. Currently, data are insufficient to recommend an optimal surveillance interval. As a result, current American Gastroenterological Association (AGA) guidelines suggest against routine use of endoscopic surveillance in patients with GIM, which is a conditional recommendation given the quality of evidence. And, in patients with GIM, the AGA suggests against routine short-interval repeat endoscopy for the purpose of risk stratification.

REFERENCES

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Question 3

Which scenario confers the highest risk of developing gastric cancer?

- A. Complete gastric intestinal metaplasia (GIM), antrum only
- B. Complete GIM, antrum and body
- C. Incomplete GIM, antrum only
- D. Incomplete GIM, antrum and body

CORRECT ANSWER: D

RATIONALE

Extensive GIM involves both the antrum and corpus or corpus alone, versus limited GIM involving only the antrum or incisura. Complete GIM resembles small intestinal epithelium phenotype on hematoxylin and eosin (H&E) staining, and incomplete GIM resembles colonic epithelium phenotype on H&E staining. The American Gastroenterological Association (AGA) technical review of GIM found that, among patients with GIM, incomplete GIM was associated with a 3.3-fold (relative risk [RR], 3.33; 95% confidence interval [CI], 1.96-5.64) higher risk of incident gastric cancer compared with complete GIM during follow-up ranging from 3 to 12.8 years. This same review identified extensive GIM associated with a nonstatistically significant 2-fold increased risk of progression compared with limited GIM (RR, 2.07; 95% CI, 0.97-4.42). Based on these data, a patient with extensive GIM with histopathology showing an incomplete phenotype would be at the highest risk of progression.

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Gupta S, Li D, El Serag HB, et al. AGA Clinical Practice Guidelines on Management of Gastric Intestinal Metaplasia. *Gastroenterology*. 2020;3:693-702. <https://doi.org/10.1053/j.gastro.2019.12.003>

Question 4

A 48-year-old woman reports daily heartburn. She has been prescribed omeprazole 40 mg once daily without benefit. After increasing her dose to 40 mg twice daily 30 minutes before breakfast and dinner, she has had a mild reduction in her frequency of heartburn but continues with symptoms a few times weekly. An upper endoscopy performed 2 years earlier for the same symptoms was normal, and esophageal biopsies at that time revealed acute inflammation consistent with reflux changes without.

What likely explains her lack of response to proton pump inhibitors (PPIs)?

- A. Insufficient potency of omeprazole to treat daily heartburn
- B. Rapid PPI metabolism
- C. Suboptimal medication adherence
- D. Unrecognized eosinophilic esophagitis

CORRECT ANSWER: B

RATIONALE

There are numerous reasons why patients with GERD symptoms might have an incomplete response to acid suppression with PPIs; these include suboptimal dosing or adherence, incorrect diagnosis, or others. In this case, the patient had biopsies that ruled out eosinophilic esophagitis. She is taking the medication appropriately, on an empty stomach 30 minutes before meals. Omeprazole is an appropriate treatment for gastroesophageal reflux disease, with no concerns regarding potency. Another explanation for incomplete response to PPI may be metabolic, as PPIs undergo metabolism by the cytochrome P450 system via the isoenzymes CYP2C19 and CYP3A4 in the liver and small intestine. The cytochrome P450 system has numerous polymorphisms, and variations in the *CYP* genes result in several different phenotypes, including ultrarapid, rapid, normal, intermediate, or poor metabolizers of PPIs. These phenotypes influence serum concentration and medication efficacy. One gain of function allele, found in 20% of both White patients and those of

Ethiopian ancestry, is responsible for ultrarapid and rapid metabolism, leading to a substantial reduction in PPI efficacy. In this case, the patient has undergone an appropriate evaluation for alternative explanations and may be a candidate for pharmacogenomic analysis to provide a personalized assessment of her medication requirements.

REFERENCE

Harris DM, Stancampiano FF, Burton MC, et al. Use of Pharmacogenomics to Guide Proton Pump Inhibitor Therapy in Clinical Practice. *Dig Dis Sci.* 2021;66(12):4120-4127. doi:10.1007/s10620-020-06814-1

Question 5

Which proton pump inhibitor (PPI) has the highest potency?

- A. Lansoprazole
- B. Omeprazole
- C. Pantoprazole
- D. Rabeprazole

CORRECT ANSWER: D

RATIONALE

Within-class switching of PPIs for patients with incomplete control of symptoms is frequently done in clinical practice. For the management of gastroesophageal reflux disease, this practice can be “considered” according to guidelines. More recent data suggest varying potencies of PPIs might be responsible for some patient’s incomplete response. When measured as omeprazole equivalents (OEs), the relative potencies of standard-dose pantoprazole, lansoprazole, omeprazole, esomeprazole, and rabeprazole have been estimated at 0.23, 0.90, 1.00, 1.60, and 1.82 OEs, respectively.

REFERENCES

Graham DY, Tansel A. Interchangeable Use of Proton Pump Inhibitors Based on Relative Potency. *Clin Gastroenterol Hepatol.* 2018;16(6):800-808.e7. doi:10.1016/j.cgh.2017.09.033

Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. *Am J Gastroenterol*. 2022;117(1):27-56. doi:10.14309/ajg.0000000000001538

Kirchheiner J, Glatt S, Fuhr U, et al. Relative potency of proton-pump inhibitors-comparison of effects on intragastric pH. *Eur J Clin Pharmacol*. 2009;65(1):19-31. doi:10.1007/s00228-008-0576-5

Question 6

A 62-year-old woman with rheumatoid arthritis reports regurgitation, heartburn, and dysphagia. She undergoes upper endoscopy, which reveals a 3-cm hiatal hernia and Los Angeles (LA) Grade D esophagitis. Previously performed esophageal function tests revealed absent contractility and a total acid exposure time of 8.2%. Her thoracic surgeon is concerned about the postoperative risks of dysphagia with hernia repair; therefore, surgery is deferred. Although improved, she continues to have symptoms of heartburn with daily lansoprazole.

Which of the following is likely to provide the best chance at symptom improvement?

- A. Adding calcium carbonate (antacid) to her current regimen
- B. Switching lansoprazole to vonoprazan
- C. Using antireflux precautions including sleeping on 2 pillows
- D. Avoiding eating spicy foods

CORRECT ANSWER: B

RATIONALE

Compared with proton pump inhibitors (PPIs), vonoprazan is a potassium-competitive acid blocker (PCAB), which inhibits acid secretion by competitively blocking availability of potassium to hydrogen-potassium ATPase. Vonoprazan is rapidly absorbed independent of eating and is not affected by CYP2C19 polymorphisms. Several

studies have compared PPIs with vonoprazan. Although vonoprazan is highly effective for treating LA Grade A and B esophagitis, so is lansoprazole, and healing rates at 8 weeks are 100% versus 99.2%, respectively. In contrast, vonoprazan healing of LA Grade C and D esophagitis at 8 weeks is 98.7% compared with 87.5% for lansoprazole. Sleeping on pillows is not a reliable way to reduce reflux, as patients often move during sleep and lose any benefit from being propped on them. Antacids would not provide superior acid inhibition compared with vonoprazan, and avoiding spicy foods would not address the underlying permissive reflux barrier that exists (hiatal hernia).

REFERENCE

Graham DY, Dore MP. Update on the Use of Vonoprazan: A Competitive Acid Blocker. *Gastroenterology*. 2018;154(3):462-466. doi:10.1053/j.gastro.2018.01.018

Question 7

A 76-year-old man with atrial fibrillation treated with long-term anticoagulation with warfarin and coronary artery disease treated with aspirin was recently admitted with melena. Upper endoscopy revealed a duodenal ulcer with visible vessel. Endoscopic therapy was performed, and he was started on twice-daily proton pump inhibitors (PPI).

Which of the following is the best monitoring approach in this patient?

- A. No monitoring of PPI side effects
- B. Baseline neurocognitive testing to evaluate for changes in memory
- C. Fasting glucose every 6 months to assess for presence of diabetes
- D. Yearly dual-energy X-ray absorptiometry scans
- E. Yearly basic metabolic profile and iron studies

CORRECT ANSWER: A

RATIONALE

There are several putative risks associated with

long-term PPI use: chronic kidney disease, dementia, vitamin and mineral deficiencies, and others. However, the overall quality of evidence to support these conclusions is low or very low, and the majority of the findings have low effect sizes that may be attributed to confounding. An American Gastroenterological Association clinical practice update recommended against routine monitoring for patients receiving long-term PPI treatment. However, data show that more than one third of gastroenterologists still check for PPI side effects at least annually in their patients.

REFERENCES

Freedberg DE, Kim LS, Yang YX. The Risks and Benefits of Long-term Use of Proton Pump Inhibitors: Expert Review and Best Practice Advice From the American Gastroenterological Association. *Gastroenterology*. 2017;152(4):706-715. doi:10.1053/j.gastro.2017.01.031

Leiman DA, Ravi K, Freedberg DE, Gyawali CP. Proton Pump Inhibitor Prescribing and Monitoring Patterns Among Gastroenterology Practitioners [published online ahead of print, 2021 Oct 4]. *J Clin Gastroenterol*. 2021;10.1097/MCG.0000000000001623. doi:10.1097/MCG.0000000000001623

Question 8

The risk most likely to be attributed to proton pump inhibitor (PPI) use is:

- A. Enteric infection
- B. Dementia
- C. Diabetes
- D. Gastric cancer
- E. Renal insufficiency

CORRECT ANSWER: A

RATIONALE

Despite the numerous side effects associated with long-term PPI use, the quality of evidence and risk of confounding from these studies limits the

ability to ascribe sufficient cause and effect between PPI use and these outcomes. However, a recent large randomized controlled trial that evaluated the use of pantoprazole versus placebo demonstrated a statistically significant difference between the pantoprazole and placebo groups only in enteric infections (1.4% vs 1.0%; odds ratio, 1.33; 95% confidence interval, 1.01-1.75). Despite a nearly double increased risk of *Clostridioides difficile* infection in the PPI group compared with the placebo group, the number of events was low, and the difference did not reach statistical significance. In the context of these data, and more recent studies suggesting an increased risk of COVID-19 in patients who take PPIs compared with those who do not, the risk of enteric infections is likely small but significantly increased among long-term PPI users.

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Freedberg DE, Kim LS, Yang YX. The Risks and Benefits of Long-term Use of Proton Pump Inhibitors: Expert Review and Best Practice Advice From the American Gastroenterological Association. *Gastroenterology*. 2017;152(4):706-715. doi:10.1053/j.gastro.2017.01.031

Moayyedi P, Eikelboom JW, Bosch J, et al. Safety of Proton Pump Inhibitors Based on a Large, Multi-Year, Randomized Trial of Patients Receiving Rivaroxaban or Aspirin. *Gastroenterology*. 2019;157(3):682-691.e2. doi:10.1053/j.gastro.2019.05.056

Question 9

A 52-year-old man presents to the emergency department after 6 months of nausea with frequent vomiting. He has noticed increasing lower extremity swelling but has lost 23 pounds in this time, which he attributes to worsening anorexia. On presentation, a complete metabolic profile reveals hypoalbuminemia. A gastroenterology consultation is performed, and upper endoscopy is notable for enlarged gastric folds. Gastric mucosal biopsies reveal prominent expansion of the gastric pits with a corkscrew, as well as cystic dilation of

glands in the basal portion of the mucosa consistent with Menetrier disease.

Menetrier disease is caused by increased signaling in which of these pathways?

- A. 5-hydroxytryptamine 3 (5HT-3) receptor
- B. Epidermal growth factor receptor (EGFR)
- C. Ganglioside GM1 receptor
- D. Histamine 2 (H2) receptor

CORRECT ANSWER: B

RATIONALE

Menetrier disease is a rare disease affecting the stomach, resulting in hypertrophied gastric folds usually in the fundus. It is characterized by excessive mucous production, hypoproteinemia, and reduced acid production (achlorhydria). At the cellular level, EGFR in foveolar mucus cells is overstimulated by its ligand, transdermal growth factor alpha, causing excess mucus secretion and nutrient malabsorption. Serotonin receptors such as 5HT-3 can modulate the activity of vagal afferents in several sites within the gastrointestinal tract. Modulation of this receptor can impact nausea, vomiting, and visceral hypersensitivity; agonism of the receptor increases nausea and vomiting and antagonism has antiemetic effects. The ganglioside GM1 receptor is activated in cholera toxin and ultimately results in intraluminal electrolyte transport and diarrhea. H2 receptors are located on parietal cells and when activated stimulate gastric acid production.

Reference

Burdick JS, Chung E, Tanner G, et al. Treatment of Ménétrier's disease with a monoclonal antibody against the epidermal growth factor receptor. *N Engl J Med*. 2000;343(23):1697-1701. doi:10.1056/NEJM200012073432305

Question 10

A 57-year-old man works as an auto mechanic. His medical history is notable for a prior cholecystec-

tomy and hyperlipidemia. He reports chronic back pain to his primary care provider and is started on nonsteroidal antiinflammatory drugs (NSAIDs) for symptom control.

Which formulation is associated with the highest risk of peptic ulcer disease complications?

- A. Diclofenac
- B. Ibuprofen
- C. Meloxicam
- D. Naproxen

CORRECT ANSWER: D

RATIONALE

NSAIDs inhibit the rate-limiting enzyme cyclooxygenase (COX) in prostaglandin synthesis. Two COX isoforms have been identified, COX-1 and COX-2. The COX-1 isoform produces cytoprotective prostaglandins and is present in most tissues, including the gastrointestinal mucosa, kidneys, and platelets. Alternatively, bacterial products and cytokines induce the expression of COX-2, and this isoform is primarily found in areas of inflammation. The therapeutic effects of NSAIDs relate to COX-2 inhibition, and gastrointestinal side effects to COX-1 inhibition. Traditional NSAIDs are nonselective, inhibiting both COX-1 and COX-2 and thus are independently associated with an increased risk of gastrointestinal ulceration and bleeding. Selective COX-2 inhibitors allow for the therapeutic effects of traditional NSAIDs, with fewer gastrointestinal side effects related to COX-1 inhibition. Diclofenac and meloxicam are selective COX-2 inhibitors and thus have a lower rate of gastrointestinal side effects than traditional NSAIDs such as ibuprofen and naproxen. Among the 2 nonselective/traditional NSAIDs listed, the risk of gastrointestinal side effects with ibuprofen is lowest, whereas the risk of naproxen is highest.

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ed formulations. *BMC Clin Pharmacol.* 2001;1:1. doi:10.1186/1472-6904-1-1

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Question 11

What is the primary mechanism by which nonsteroidal anti-inflammatory drugs (NSAIDs) increase the risk of peptic ulcer disease?

- A. Decreased prostaglandin synthesis
- B. Down-regulation of gastric acid production
- C. Increased gastric blood flow
- D. Increased production of gastric mucous layer

CORRECT ANSWER: A

RATIONALE

NSAIDs have multiple effects on the gastrointestinal tract. Although they can lead to direct epithelial injury, it is primarily through COX-mediated processes that NSAIDs can affect many of these gastroprotective effects, including decreasing prostaglandin synthesis. Also, they upregulate gastric acid production, reduce production of the gastric mucous layer, and reduce gastric blood flow.

REFERENCE

Bjarnason I, Scarpignato C, Holmgren E, Olszewski M, Rainsford KD, Lanas A. Mechanisms of Damage to the Gastrointestinal Tract From Nonsteroidal Anti-Inflammatory Drugs. *Gastroen-*

terology. 2018;154(3):500-514. doi:10.1053/j.gastro.2017.10.049

Question 12

A 51-year-old morbidly obese woman is referred to the gastroenterology clinic for new-onset iron-deficiency anemia. She takes no medications. At 50 years of age, she underwent an average-risk screening colonoscopy, which was normal except for left-sided diverticulosis and hemorrhoids. An upper endoscopy is performed. Biopsies of normal-appearing gastric and duodenal mucosa do not reveal any histologic abnormalities. She is noted to have a 5 cm hiatal hernia with multiple small shallow erosions located within the hernia sac.

Which of the following is the most likely underlying etiology of this patient's condition?

- A. *Helicobacter pylori* infection
- B. Increased gastric acid production
- C. Mechanical trauma from hernia sac
- D. Nonsteroidal antiinflammatory drug use
- E. Tobacco use

CORRECT ANSWER: C

RATIONALE

Cameron lesions are erosions or ulcerations at the level of the diaphragmatic hiatus that are found within a hiatal hernia. In the context of an evaluation of iron-deficiency anemia, upper endoscopy should be performed and can help identify several etiologies including celiac disease and *H pylori* infection. In this case, duodenal and gastric biopsies are negative for either. The presence of Cameron lesions may also be a source of iron deficiency identifiable on endoscopy and are more common in the presence of a larger hiatal hernia (ie, 5 cm in size or greater). As a result, these are typically associated with mechanical trauma from the hernia sac. However, data also reveal the use of nonsteroidal antiinflammatory therapy as a risk factor for developing Cameron lesions. This patient is on no medications, so this is less likely. In

contrast, the use of tobacco has not been identified as a source of such lesions.

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Question 13

A 58-year-old woman with a history of hypothyroidism on thyroid replacement hormone saw her primary care provider to assess for a new tingling sensation in her fingers. Blood work revealed megaloblastic anemia with a low vitamin B12 level. She is referred to gastroenterology.

Which of the following is the most sensitive test to identify autoimmune atrophic gastritis as the cause of her vitamin B12 deficiency?

- A. Anti-intrinsic factor antibody
- B. Anti-parietal cell antibody
- C. Schilling test
- D. Serum homocysteine level

CORRECT ANSWER: B

RATIONALE

Autoimmune metaplastic atrophic gastritis can occur in the context of polyglandular autoimmune syndrome. When present, autoimmune metaplastic atrophic gastritis can progress to pernicious anemia that is characterized by low levels of vitamin B12, due to parietal cell dropout and resultant loss of intrinsic factor. Intrinsic factor is required for vitamin B12 to be absorbed in the terminal ileum. As a result, both anti-parietal cell and anti-intrinsic factor antibodies are used to determine

the cause of B12 deficiency. However, the sensitivity for the former is 80% compared with 50% for the latter. The Schilling test can provide insight into the etiology of B12 deficiency, including problems with intrinsic factor production versus malabsorption; however, it is rarely available and therefore not the ideal test. The serum homocysteine level is highly sensitive to detect B12 deficiency but cannot identify a cause and may be affected by the presence of renal insufficiency.

REFERENCE

Stabler SP. Clinical practice. Vitamin B12 deficiency. *N Engl J Med*. 2013;368(2):149-160. doi:10.1056/NEJMcp1113996

Question 14

A 42-year-old man with no chronic medical problems is referred for open-access upper endoscopy for abdominal pain. He has had no relief with dietary modifications or over-the-counter therapy such as peppermint oil. His pain is described as burning in character and located in the epigastric area. He has not had any weight loss, though he does report early satiety. He previously tried a proton pump inhibitor for 4 weeks without benefit. The mucosa is normal appearing on endoscopy; therefore, what is the best approach for tissue sampling?

- A. Biopsy the gastric body and antrum in separate jars
- B. Biopsy the gastric body, antrum, and incisura
- C. Biopsy the esophagus, stomach, and duodenum
- D. Biopsy the duodenum

CORRECT ANSWER: B

RATIONALE

Many patients with dyspepsia symptoms, including epigastric pain and burning, early satiety, and postprandial fullness, undergo upper endoscopy. In immunocompetent patients without an identifiable lesion and in patients with dyspepsia, American Gastroenterological Association (AGA)

guidelines recommend against biopsies of the esophagus or esophagogastric junction. They also recommend against obtaining biopsies from the duodenum when no symptoms or signs suggest celiac disease. The AGA does recommend obtaining gastric biopsies in this context, however, to evaluate for *Helicobacter pylori* infection. Although special stains are not required, biopsies should be obtained according to the Sydney protocol, obtaining samples from the gastric body, antrum, and incisura. The Sydney protocol was shown to identify 100% of *H pylori* infections in one study. The AGA recommends against using separate jars as this is unnecessary and costly.

REFERENCE

Yang YX, Brill J, Krishnan P, Leontiadis G; American Gastroenterological Association Clinical Practice Guidelines Committee. American Gastroenterological Association Institute Guideline on the Role of Upper Gastrointestinal Biopsy to Evaluate Dyspepsia in the Adult Patient in the Absence of Visible Mucosal Lesions. *Gastroenterology*. 2015;149(4):1082-1087. doi:10.1053/j.gastro.2015.07.039

Question 15

A 41-year-old man has heartburn and regurgitation. After his primary care provider starts him on daily PPI his symptoms of heartburn resolve, but he continues to have intermittent episodes of volume regurgitation. A barium swallow revealed a 3-cm hiatal hernia. He would like to avoid surgical intervention. Which medicine would you recommend to reduce ongoing symptoms despite his PPI?

- A. Alginate
- B. Calcium carbonate (antacid)
- C. Histamine 2 (H₂) receptor antagonist
- D. Viscous lidocaine

CORRECT ANSWER: A

RATIONALE

Gastric acid production is stimulated by multiple

mechanisms, including via vagal inputs even at the thought of ingesting a meal. This acid production is buffered during meal consumption. However, a layer of unbuffered contents referred to as the acid pocket sits within the proximal stomach in the area of the cardia and fundus. Buffering of, and potentially physically inhibiting, this layer with the use of alginates can reduce the symptoms of gastroesophageal reflux after meals. In contrast, viscous lidocaine would only numb the mouth and chest. Although the use of antacids and H₂ receptor antagonists could buffer and reduce acid secretion, respectively, the current ongoing symptoms are more likely mechanical in nature rather than secretory.

REFERENCE

Rohof WO, Bennink RJ, Smout AJ, Thomas E, Boeckxstaens GE. An alginate-antacid formulation localizes to the acid pocket to reduce acid reflux in patients with gastroesophageal reflux disease. *Clin Gastroenterol Hepatol*. 2013;11(12):1585-e90. doi:10.1016/j.cgh.2013.04.046

Question 16

A 75-year-old man with a history of remote peptic ulcer disease previously underwent partial gastrectomy with a gastrojejunostomy anastomosis (Billroth II) for refractory ulceration with bleeding. He has a history of hypertension and nonobstructive coronary artery disease. Several years after surgery he developed dyspepsia, which was successfully treated with over-the-counter antacids, and the original surgical report does not describe a vagotomy being performed. He had been treated with pantoprazole 20 mg daily, but this did not resolve his symptoms. Over the ensuing years, he had several admissions for gastrointestinal bleeding before eventually being placed on a cumulative daily dose of 80 mg of omeprazole. He is referred to the gastroenterology clinic and undergoes an upper endoscopy, which revealed an anastomotic and jejunal ulcer. A fasting serum gastrin level was 195 pg/mL (reference range, <100 pg/mL).

The best next step in evaluation is:

Which of the following scoring systems provides the single best estimate of whether he would benefit from hospital admission and early endoscopy (within 24 hours)?

- A. Secretin stimulation test
- B. Octreotide nuclear medicine scan
- C. Empirically increase omeprazole to three times daily dosing
- D. Exploratory laparotomy

CORRECT ANSWER: A

RATIONALE

This patient's persistent ulcerations are likely due to retained antrum from a prior Billroth II operation. In this scenario, a portion of the antrum is inadvertently left behind after surgery and, when chronically bathed in alkaline fluid in the excluded portion, leads to unopposed gastrin hypersecretion and gastric acid production. A secretin stimulation test can differentiate between hypergastrinemia from gastrinoma or retained antrum. If an octreotide nuclear medicine scan were performed and found to be negative, it would neither confirm the etiology nor exclude other diagnoses within the differential. There is no evidence of perforation, so surgery at this time is premature. Increasing his proton pump inhibitor further does not treat the underlying predisposing cause.

REFERENCE

Gibril F, Lindeman RJ, Abou-Saif A, et al. Retained gastric antrum syndrome: a forgotten, treatable cause of refractory peptic ulcer disease. *Dig Dis Sci*. 2001;46(3):610-617. doi:10.1023/a:1005667719847

Question 17

A 50-year-old man with long-standing heartburn and a father who died of esophageal adenocarcinoma undergoes an upper endoscopy to screen for Barrett esophagus. He developed symptoms of gastroesophageal reflux disease while in graduate school and has been taking daily pro-

ton pump inhibitors (PPIs) for 20 years.

In addition to a 4 cm segment of Barrett esophagus, multiple pearly white polyps with a lacy reticular vascular pattern are present in the gastric body, ranging in size from 1 mm to 1.5 cm.

Which factor increases the risk of dysplasia in fundic gland polyps?

- A. Antral gastritis
- B. Barrett's esophagus
- C. Lynch syndrome
- D. Small size of polyp

CORRECT ANSWER: A

RATIONALE

Fundic gland polyps are commonly encountered during upper endoscopy, especially among long-term PPI users. These polyps are generally considered to have low risk of malignant transformation, based on the chemopreventive properties of PPIs. However, dysplasia is associated with presence of antral gastritis, familial adenomatous polyposis syndrome, and increasing size of the largest fundic gland polyp. Barrett's esophagus, Lynch syndrome, and small fundic gland polyp size are not associated with the development of dysplastic fundic gland polyps.

REFERENCE

Bianchi LK, Burke CA, Bennett AE, Lopez R, Hasson H, Church JM. Fundic gland polyp dysplasia is common in familial adenomatous polyposis. *Clin Gastroenterol Hepatol*. 2008;6(2):180-185. doi:10.1016/j.cgh.2007.11.018

Question 18

A 54-year-old woman reports numbness in both feet. She has a history of autoimmune thyroiditis, and a sister has type 1 diabetes. Her primary care provider checks her screening laboratory tests and finds a macrocytic anemia and serum B12 level below the normal range. Anti-intrinsic factor antibodies are positive.

This patient is at risk of developing which of the following?

- A. Esophageal adenocarcinoma
- B. Noncardia gastric adenocarcinoma
- C. Pancreatic ductal adenocarcinoma
- D. Rectal cancer

CORRECT ANSWER: B

RATIONALE

Pernicious anemia is the most common cause of B12 deficiency, which results from chronic atrophic gastritis from autoantibodies leading to the loss of parietal cells. In the absence of parietal cells, a reduction in intrinsic factor limits B12 absorption. Chronic inflammation, especially in the presence of *Helicobacter pylori*, is suspected to increase the risk of gastric carcinoids as well as noncardia gastric adenocarcinoma in these patients. The presence of pernicious anemia is also associated with an increased risk of both gastrointestinal and nongastrointestinal malignancies, such as esophageal squamous cell cancer, small intestinal cancer, and multiple myeloma. Studies have not reliably demonstrated an increased risk associated with esophageal adenocarcinoma, pancreatic ductal adenocarcinoma, or rectal cancer.

REFERENCES

Murphy G, Dawsey SM, Engels EA, et al. Cancer Risk After Pernicious Anemia in the US Elderly Population. *Clin Gastroenterol Hepatol*. 2015;13(13):2282-9.e94. doi:10.1016/j.cgh.2015.05.040

Shah P, Rhim AD, Haynes K, Hwang WT, Yang YX. Diagnosis of pernicious anemia and the risk of pancreatic cancer. *Pancreas*. 2014;43(3):422-426. doi:10.1097/MPA.000000000000054

Question 19

A 26-year-old woman with a history of depression presents to the gastroenterology clinic after referral from student health for increasing

epigastric abdominal discomfort. She notes an increase in stress recently as she is studying for her first semester law school exams. Her pain has been present on most days and is also associated with early satiety. She cannot identify any specific triggers such as food intake or bowel pattern. She has no prior medical problems, and her weight is stable despite these symptoms. A trial of over-the-counter proton pump inhibitors for six weeks has not been helpful, and a basic metabolic profile, thyroid studies, and a complete blood count were all normal. An upper endoscopy was normal with biopsies negative for *Helicobacter pylori*, and a previously ordered gastric emptying scan was normal. The patient presents now for a follow up appointment. Which therapeutic mechanism is most likely to reduce this patient's symptoms?

- A. Anxiolysis with a benzodiazepine
- B. Appetite stimulation with megestrol acetate
- C. Fundic relaxation and accommodation with buspirone
- D. Gastric emptying time reduction with metoclopramide

CORRECT ANSWER: C

RATIONALE

This patient has functional dyspepsia, which is defined by the Rome IV criteria as the presence of 1 or more of the following symptoms: postprandial fullness, early satiation, epigastric pain or epigastric burning, and no evidence of structural disease (including at upper endoscopy) to explain the symptoms. Functional dyspepsia can be treated first with a trial of proton pump inhibitors and, if ineffective, tricyclic antidepressants or prokinetic agents. Fundic relaxants may play a role in improvement in early satiation especially. Benzodiazepines are not appropriate treatment options given their side effect profile and potential for dependence. Appetite stimulation with megestrol will not improve the symptoms of dyspepsia. Although metoclopramide can be used for functional dyspepsia, its use is

limited by potential neurologic side effects. This patient has already been shown to have normal gastric emptying.

Buspirone is a serotonin 1A (5-HT_{1A}) agonist that has clinical efficacy for patients with anxiety and has been shown to be superior to placebo in alleviating symptoms of functional dyspepsia. The symptoms most improved include postprandial fullness, bloating, and early satiety, rather than abdominal pain. There may be several mechanisms by which the therapeutic effects occur, and they are likely independent of the anxiolytic properties alone based on the lack of correlation between anxiety scores and symptom improvement. Patients with functional dyspepsia showed improvement in symptoms, which were associated with a delay in liquid gastric emptying rate and an increase in meal-induced gastric accommodation.

REFERENCES

Ford AC, Mahadeva S, Carbone MF, Lacy BE, Talley NJ. Functional dyspepsia. *Lancet*. 2020;396(10263):1689-1702. doi:10.1016/S0140-6736(20)30469-4

Tack J, Janssen P, Masaoka T, Farré R, Van Oudenhove L. Efficacy of buspirone, a fundus-relaxing drug, in patients with functional dyspepsia. *Clin Gastroenterol Hepatol*. 2012;10(11):1239-1245. doi:10.1016/j.cgh.2012.06.036

Question 20

A 44-year-old woman with morbid obesity, type 2 diabetes, and gastroesophageal reflux undergoes Roux-en-Y gastric bypass. The initial postoperative period was noted for a weight loss of 42 kg from her maximal weight. At her follow-up visit with bariatric surgery, she mentions weakness and epigastric abdominal discomfort. An upper gastrointestinal series with barium reveals no fistula and otherwise normal postoperative anatomy. Her symptoms persist and an upper endoscopy is performed, revealing a linear ulcer along the margin of the gastroenterostomy.

Which of the following is a risk factor for the development of this patient's condition?

- A. Hypertension
- B. Long gastric pouch
- C. Proton pump inhibitor use
- D. Weight loss of >25 kg after surgery

CORRECT ANSWER: B

RATIONALE

Relative ischemia to the gastroenterostomy is a primary risk factor for the development of marginal ulcer in patients with a history of Roux-en-Y gastric bypass. This risk is increased in patients who smoke, use nonsteroid antiinflammatory drugs, or have diabetes. A short gastric pouch is associated with a reduced risk of marginal ulcer. Proton pump inhibitor use has been shown to decrease the risk of ulceration, not increase it. The degree of weight loss has not been shown to correlate with risk of marginal ulcer.

REFERENCES

Azagury DE, Abu Dayyeh BK, Greenwalt IT, Thompson CC. Marginal ulceration after Roux-en-Y gastric bypass surgery: characteristics, risk factors, treatment, and outcomes. *Endoscopy*. 2011;43(11):950-954. doi:10.1055/s-0030-1256951

Coblijn UK, Goucham AB, Lagarde SM, Kuiken SD, van Wagensveld BA. Development of ulcer disease after Roux-en-Y gastric bypass, incidence, risk factors, and patient presentation: a systematic review. *Obes Surg*. 2014;24(2):299-309. doi:10.1007/s11695-013-1118-5

Question 21

A 70-year-old man with worsening dyspnea is noted to have a microcytic anemia by his primary care provider. He also admits to intermittent early satiety and epigastric abdominal pain after meals. A screening colonoscopy was normal 11 months ago; therefore, he is referred for upper endoscopy. The examination is notable for a large, hyperemic

pedunculated antral polyp with eroded surface epithelium. The lesion is removed with hot snare polypectomy, and pathology confirms a hyperplastic polyp. These polyps are proliferations of which gastric cell type:

- A. Chief
- B. Enterochromaffin-like
- C. Foveolar
- D. Parietal

CORRECT ANSWER: C

RATIONALE

The patient has evidence of a hyperplastic polyp, which can result from inflammatory proliferation of mucous producing foveolar cells often in the setting of chronic bile exposure. This finding frequently is associated with mucosal atrophy but may be seen in the absence of autoimmune gastritis or *Helicobacter pylori* infection. Iron-deficiency anemia and intermittent gastric outlet obstruction due to prolapsing of large hyperplastic polyps has been described. Chief, enterochromaffin-like, and parietal cells secrete pepsinogen, histamine, and gastric acid, respectively.

REFERENCE

Shaib YH, Rugge M, Graham DY, Genta RM. Management of gastric polyps: an endoscopy-based approach. *Clin Gastroenterol Hepatol*. 2013;11(11):1374-1384. doi:10.1016/j.cgh.2013.03.019

Question 22

A 39-year-old woman without a significant past medical history is admitted to the trauma intensive care unit after sustaining multiple injuries from a motor vehicle crash. Due to maxillofacial injuries, she is started on mechanical ventilation and initially receives total parenteral nutrition. She is also started on stress-dose steroids on admission.

She develops mild renal insufficiency and later is found to have a new upper extremity deep venous

thrombosis, for which she receives therapeutic anticoagulation. Which factor most contributes to her risk of developing gastrointestinal bleeding during this hospitalization?

- A. Anticoagulation therapy
- B. Corticosteroid therapy
- C. Mechanical ventilation
- D. Renal failure
- E. Parenteral nutrition

CORRECT ANSWER: C

RATIONALE

Use of mechanical ventilation for more than 48 hours is an independent risk factor for gastrointestinal bleeding in the context of critical illness and warrants prophylaxis with proton pump inhibitors. Neither renal failure nor the use of anticoagulants, corticosteroids, or parenteral nutrition is an independent risk factor for developing gastrointestinal bleeding.

REFERENCE

Cook DJ, Fuller HD, Guyatt GH, et al. Risk factors for gastrointestinal bleeding in critically ill patients. Canadian Critical Care Trials Group. *N Engl J Med*. 1994;330(6):377-381. doi:10.1056/NEJM199402103300601

Question 23

A 59-year-old man with a prior appendectomy and autoimmune metaplastic atrophic gastritis is admitted to the hospital with shortness of breath and fatigue. His work-up reveals anemia, and his examination is notable for melena. He undergoes upper endoscopy, which reveals thinning of the rugal folds and an atrophic-appearing stomach. There is a 2-cm ulcerated lesion in the gastric body.

Biopsies of the ulcer reveal features consistent with a gastric neuroendocrine tumor.

What is the risk of malignancy in this type of gastric carcinoid tumor?

- A. <5%
- B. 10%-15%
- C. 30%
- D. >50%

CORRECT ANSWER: A

RATIONALE

Gastric carcinoids arise in enterochromaffin-like (ECL) cells. This case describes a type 1 gastric carcinoid, which is the most common type of gastric carcinoid and is most commonly associated with chronic atrophic gastritis. They generally have the lowest metastatic risk at less than 5%. Type 2 gastric carcinoids are the least common type of gastric carcinoids and associated with Zollinger-Ellison syndrome and MEN-1 (multiple endocrine neoplasia, type 1) syndrome. They have a metastatic risk of approximately 10%. Sporadic, or type 3, gastric carcinoids have the highest malignant potential with a metastatic risk greater than 50%.

REFERENCES

Basuroy R, Srirajaskanthan R, Prachalias A, Quaglia A, Ramage JK. Review article: the investigation and management of gastric neuroendocrine tumours. *Aliment Pharmacol Ther*. 2014;39(10):1071-1084. doi:10.1111/apt.12698

Delle Fave G, O'Toole D, Sundin A, et al. ENETS Consensus Guidelines Update for Gastroduodenal Neuroendocrine Neoplasms. *Neuroendocrinology*. 2016;103(2):119-124. doi:10.1159/000443168

Question 24

A 42-year-old woman with a history of anxiety presents with a year of globus symptoms. She denies dysphagia, heartburn, and regurgitation. A laryngoscopy performed a year earlier was normal except for arytenoid erythema for which she was started on 40 mg daily of omeprazole. Her symptoms continued despite appropriate use and adherence. As a result, her primary care provider increased her dose to a total of 80 mg daily. Despite this change, her symptoms remain, and she is

referred to the gastroenterology clinic for further management. You are planning an upper endoscopy and wireless pH testing, to be done off of acid suppression, but she is hesitant to stop her omeprazole because every other time she did so, she developed severe heartburn and chest discomfort. You explain that her difficulty stopping a proton pump inhibitor (PPI) is likely due to:

- A. Atypical gastroesophageal reflux disease
- B. Rebound hypergastrinemia
- C. Refractory gastroesophageal reflux disease
- D. Zollinger-Ellison syndrome

CORRECT ANSWER: B

RATIONALE

Rebound hypergastrinemia can cause acute symptoms of gastroesophageal reflux disease (GERD) after discontinuing PPIs abruptly. This is usually temporary, and symptoms can be ameliorated with the use of on-demand acid suppression (such as histamine 2 receptor antagonists) or tapering of PPIs. Atypical GERD is often referred to as extraesophageal GERD, and globus is a complaint attributed to this constellation of symptoms; however, that would not explain the new-onset heartburn and chest pain after stopping PPIs acutely. The finding of arytenoid erythema is not specific for GERD, and the absence of esophageal symptoms before or after initiating PPIs makes this diagnosis unlikely. Refractory GERD would present as symptoms despite maximal-dose PPI; in this case the symptoms occurred with abrupt withdrawal of PPI, not despite therapy. It is unlikely in this patient with no other symptoms consistent with peptic ulcer disease or ongoing GERD that the underlying issue is a gastrinoma (Zollinger-Ellison syndrome).

REFERENCES

Lødrup AB, Reimer C, Bytzer P. Systematic review: symptoms of rebound acid hypersecretion following proton pump inhibitor treatment. *Scand J Gastroenterol*. 2013;48(5):515-522. doi:10.3109/00365521.2012.746395

Waldum HL, Qvigstad G, Fossmark R, Kleve-land PM, Sandvik AK. Rebound acid hypersecretion from a physiological, pathophysiological and clinical viewpoint. *Scand J Gastroenterol*. 2010;45(4):389-394. doi:10.3109/00365520903477348

Question 25

A 42-year-old man with a history of 2 duodenal ulcer bleeds in the past year presents to the gastroenterology clinic after a recent hospitalization for gastrointestinal bleeding. He was noted on endoscopy to have erosive esophagitis and 3 clean-based ulcers in the third portion of the duodenum, despite taking a daily proton pump inhibitor (PPI) at home. He does not take nonsteroidal antiinflammatory drugs, and gastric biopsies were negative for *H pylori*. He is adherent to his PPI. He also reports frequent bowel movements and has lost 15 pounds over the last 9 months. His gastrin level during hospitalization was 521 pg/mL (reference range, <100 pg/mL).

Which of the following is the next best step?

- A. Check chromogranin A level
- B. Order ⁶⁸Gallium-labeled DOTATATE positron emission tomography/computed tomography (PET/CT) scan
- C. Refer for endoscopic ultrasound (EUS)
- D. Withdraw PPI and perform gastric acid analysis

CORRECT ANSWER: D

RATIONALE

This patient presents with diarrhea, esophagitis, and duodenal ulcers, as well as elevated gastrin level, which is consistent with Zollinger-Ellison syndrome (ZES) due to a gastrinoma. The most accurate means to diagnose ZES is through gastric acid analysis after careful withdrawal of antisecretory therapy. Stopping PPIs should be done with caution with clear instructions for management, including bridging with scheduled histamine 2

receptor antagonist administration. An analysis of basal acid output (BAO) can confirm the diagnosis, with levels greater than 15 mEq/h in the presence of any level of hypergastrinemia being pathognomonic of ZES. Serum chromogranin A is a marker of neuroendocrine tumors, but it is not specific for a gastrinoma, and the level can be confounded by a number of situations including use of PPI as well as chronic liver or renal disease. A radiographic study to identify a gastrinoma can be helpful but is only 70% sensitive for a primary tumor, and a negative study would not exclude ZES in this case. EUS or PET/CT for localization would be premature without first confirming the presence of inappropriate hypergastrinemia.

REFERENCE

Metz DC. Diagnosis of the Zollinger–Ellison syndrome. *Clin Gastroenterol Hepatol*. 2012;10(2):126-130. doi:10.1016/j.cgh.2011.07.012

Question 26

Which of the following suppresses gastric acid production?

- A. Acetylcholine
- B. Gastrin
- C. Histamine
- D. Somatostatin

CORRECT ANSWER: D

RATIONALE

Gastric acid is stimulated by 3 substances: gastrin, histamine, and acetylcholine. Somatostatin acts as a feedback mechanism to suppress acid production, as does acid in the stomach itself.

REFERENCE

Schubert ML, Kaunitz JD. Gastric Secretion. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management*, 10th ed. Philadelphia, PA: Elsevier Saunders, 2015.

Question 27

A 58-year-old woman presents to the clinic for follow-up of dyspepsia and reflux. She underwent a prior endoscopy notable for erosive gastropathy and Los Angeles B reflux esophagitis, with complete resolution of symptoms on omeprazole 40 mg once daily. Unfortunately, she has a strong family history of dementia and kidney disease and felt strongly that she did not want to continue long-term proton pump inhibitor therapy. She started a combination of other antacid therapies with eventual control of symptoms on a combination of alginates, famotidine, misoprostol, and sucralfate.

However, although her dyspepsia is well-controlled, she now has significant diarrhea. Stool studies for infection and inflammation are negative.

Which of the medications is the likely cause of her diarrhea?

- A. Alginates
- B. Famotidine
- C. Misoprostol
- D. Sucralfate

CORRECT ANSWER: C

RATIONALE

The 4 agents listed above all have benefit in modulation of acid production, buffering of existing acid, or enhancement of gastric protective barrier function—and all are reasonable treatment options for this patient. All 4 agents, however, do have some potential adverse effects that need to be considered, but misoprostol is the only one linked with diarrhea, which is in fact the most commonly reported adverse effect for this medication.

REFERENCES

Kim J, Blackett JW, Jodorkovsky D. Strategies for Effective Discontinuation of Proton Pump Inhibitors. *Curr Gastroenterol Rep*. 2018;20(6):27. Published 2018 May 16. doi:10.1007/s11894-018-0632-y

Krugh M, Maani CV. Misoprostol. [Updated 2021 Jul 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK539873/>

Question 28

A 70-year-old woman presents to the clinic with dyspepsia and reflux. She notes being treated for these conditions in the past with clear symptom improvement, followed by gradual recurrence of symptoms several weeks later. However, she does not recall which medication she was treated with.

Which of the following antacid therapies is most likely to be associated with tachyphylaxis?

- A. Famotidine
- B. Misoprostol
- C. Omeprazole
- D. Sucralfate

CORRECT ANSWER: A

RATIONALE

All 4 of these therapies have actions that affect acid production or gastric protective mechanisms. However, the only agent listed that is associated with tachyphylaxis is famotidine. Histamine-receptor blockers affect 1 of the 3 pathways that stimulate acid production. They are quite effective when used short-term, but compensation and upregulation of the other associated pathways for acid production and tachyphylaxis occurs with prolonged use of histamine-receptor blockers. Proton pump inhibitors are not believed to have this property, as there is no other means for acid production other than the proton pump.

REFERENCE

McRorie JW, Kirby JA, Miner PB. Histamine2-receptor antagonists: Rapid development of tachyphylaxis with repeat dosing. *World J Gastrointest Pharmacol Ther*. 2014;5(2):57-62. doi:10.4292/wjgpt.v5.i2.57

Question 29

A 25-year-old man presents to the clinic with profound muscle cramps and weakness. He has been in good health until 8 weeks ago when he developed severe abdominal pain. He went to the local drugstore and picked up several over-the-counter agents that were marketed to treat abdominal discomfort. His abdominal discomfort is now completely resolved, but he has developed horrible muscle cramps and weakness. On examination you note significant hyperreflexia. Which of his over-the-counter medications is most likely responsible for his current symptoms?

- A. Aluminum hydroxide
- B. Calcium carbonate
- C. Famotidine
- D. Omeprazole

CORRECT ANSWER: D

RATIONALE

The symptoms described in this presentation are classic for hypomagnesemia, which is a rare but potentially severe complication from proton pump inhibitor use. The other agents would not be expected to cause significant electrolyte imbalances and would be unlikely to present with similar adverse effects.

REFERENCE

William JH, Danziger J. Magnesium Deficiency and Proton-Pump Inhibitor Use: A Clinical Review. *J Clin Pharmacol*. 2016;56(6):660-668. doi:10.1002/jcph.672

Question 30

An 80-year-old woman on long-term omeprazole presents for evaluation of B12 deficiency. She has no symptoms at the time of evaluation, but her B12 level has been persistently low on routine laboratory testing.

What is the most likely mechanism that explains her low serum B12 level?

- A. Acid suppression affecting cleavage of cobalamin from dietary protein
- B. Decreased production of haptocorrin (R-protein) affecting B12 binding
- C. Impaired cleavage of the B12-intrinsic factor complex in the small bowel
- D. Reduced secretion of intrinsic factor due to parietal cell suppression

CORRECT ANSWER: A

RATIONALE

Chronic proton pump inhibitor use has been linked to B12 deficiency. Although many potential mechanisms have been implicated, the current leading theory is that acid suppression reduces the cleavage of cobalamin from dietary proteins (as pepsin is not as readily activated outside of an acidic milieu), reducing the ability of cobalamin to bind in the stomach with intrinsic factor. If small intestinal bacterial overgrowth is present, then cleavage of the B12-intrinsic factor complex could potentially be affected, but this mechanism is more controversial and believed to be less of a factor than answer A. Haptocorrin production is not affected by proton pump inhibition, nor is intrinsic factor production.

REFERENCE

Stabler SP. Clinical practice. Vitamin B12 deficiency. *N Engl J Med*. 2013;368(2):149-160. doi:10.1056/NEJMcp1113996

Question 31

A 32-year-old man with recent ibuprofen use for back pain and history of smoking (20 pack-years), eosinophilic esophagitis, and asthma presents with 2 weeks of epigastric abdominal pain that is worse upon eating. While in the emergency department, he vomits bright red blood. While investigation and fluid resuscitation are arranged, you are called to consider urgent endoscopy for evaluation and potential hemostasis. In addition to intravenous proton pump inhibitors, which of the following agents would be reasonable to suggest at this time?

- A. Ceftriaxone
- B. Erythromycin
- C. Famotidine
- D. Sucralfate

CORRECT ANSWER: B

RATIONALE

Intravenous erythromycin is reasonable to consider in patients with brisk upper gastrointestinal bleeding before endoscopy, with the hypothesis that this will speed gastric emptying and may allow better visualization and more optimal evaluation and therapy, with decreased need for repeat endoscopy thereafter. Antibiotics such as ceftriaxone are warranted for gastrointestinal bleeding in cirrhotic patients, but there is no indication that this patient has cirrhosis. Famotidine and sucralfate are not indicated in the acute setting of peptic ulcer bleeding.

REFERENCE

Barkun AN, Bardou M, Kuipers EJ, et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. *Ann Intern Med*. 2010;152(2):101-113. doi:10.7326/0003-4819-152-2-201001190-00009

Question 32

A 60-year-old woman presents with abdominal pain, nausea, and weight loss. Endoscopy is performed and shows active gastritis with a duodenal ulcer. Biopsies show *Helicobacter pylori* (*H pylori*) infection, and she is treated with quadruple therapy. Symptoms initially improve but then recur.

What would be the most sensitive test to evaluate whether she still has active *H pylori* infection?

- A. Endoscopy with biopsies
- B. Gastric tissue culture
- C. Serum antibody test
- D. Urease breath test

CORRECT ANSWER: D

RATIONALE

Numerous tests exist to evaluate for potential *H pylori* infection, and these tests have their pros and cons. Urease breath test and *H pylori* stool antigen evaluation, when performed off proton pump inhibitor therapy, are both believed to be greater than 95% sensitive and would be the best options for this situation. Serology is specific but does not differentiate between active and prior infection and would not be appropriate in this case. Biopsies for histopathology or culture would both be specific but are less sensitive than urease breath testing and stool antigen testing.

REFERENCE

El-Serag HB, Kao JY, Kanwal F, et al. Houston Consensus Conference on Testing for Helicobacter pylori Infection in the United States. *Clin Gastroenterol Hepatol*. 2018;16(7):992-1002.e6. doi:10.1016/j.cgh.2018.03.013

Question 33

A 25-year-old man presents to see you in the clinic with incidentally discovered *Helicobacter pylori* (*H pylori*) infection. He denies symptoms at the time of your appointment and is weighing the pros and cons of eradication therapy. He wants to discuss potential risks of chronic *H pylori* infection but also wants to discuss whether there could be any theoretical protective benefits. During this conversation, you mention that the prevalence of *H pylori* is inversely associated with which of the following conditions?

- A. Dyspepsia
- B. Esophageal adenocarcinoma
- C. Gastric adenocarcinoma
- D. MALT lymphoma

CORRECT ANSWER: B

RATIONALE

Chronic *H pylori* is associated with dyspepsia,

gastric cancer, and MALT (mucosa-associated lymphatic tissue) lymphoma; however, there are suggestions that it may be inversely associated with other conditions including esophageal adenocarcinoma and potentially asthma, food allergies, and autism. It is not clear that there is a protective effect per se, but there is an inverse association that factors into treatment decisions in patients with incidentally discovered asymptomatic *H. pylori* cases.

REFERENCE

Islami F, Kamangar F. *Helicobacter pylori* and esophageal cancer risk: a meta-analysis. *Cancer Prev Res (Phila)*. 2008;1(5):329-338. doi:10.1158/1940-6207.CAPR-08-0109

Question 34

A 52-year-old man with a history of hypertension, asthma, and hyperthyroidism presents with abdominal pain and weight loss. Endoscopy shows a gastric ulcer with biopsy confirmation of *Helicobacter pylori* infection. He is taking ibuprofen, metoprolol, and a fluticasone inhaler and notes a distant allergy to penicillin. Which of the following treatment regimens for *Helicobacter pylori* infection would be most appropriate as first-line therapy in this case?

- A. Omeprazole, bismuth, tetracycline, and metronidazole for 14 days
- B. Omeprazole, clarithromycin, and amoxicillin for 14 days
- C. Pantoprazole, clarithromycin, and metronidazole for 14 days
- D. Pantoprazole, rifabutin, metronidazole and levofloxacin for 14 days

CORRECT ANSWER: A

RATIONALE

Because of increasing antibiotic resistance worldwide, most authorities now recommend bismuth-based quadruple therapy as the initial therapy of choice; in this example, the history of a penicillin

allergy would make standard triple-therapy less appealing and reinforce omeprazole, bismuth, tetracycline, and metronidazole as the best option of the above choices. The standard treatment regimen is 14 days, although the rifabutin triple-therapy option can be used for a 10-day course.

REFERENCE

Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection. *Am J Gastroenterol*. 2017;112(2):212-239. doi:10.1038/ajg.2016.563

Question 35

A 40-year-old woman presents to the clinic with abdominal pain and melena. She has a past medical history notable for asthma, multiple food allergies, irritable bowel syndrome, systemic mastocytosis, and Crohn's disease. Evaluation shows diffuse duodenal ulcerations. Basal acid output is measured and found to be elevated. Which of her medical conditions is most likely to contribute to an acid hypersecretory state?

- A. Asthma
- B. Crohn's disease
- C. Irritable bowel syndrome
- D. Systemic mastocytosis

CORRECT ANSWER: D

RATIONALE

Acid hypersecretion can occur with systemic mastocytosis due to excessive histamine production. Histamine is the most important stimulator of acid secretion. It is released by enterochromaffin-like cells and stimulates parietal cells to secrete acid. Hypersecretion can also be associated with other disease states including neuroendocrine tumors and basophilic leukemia. Asthma, Crohn's disease, and irritable bowel syndrome are not generally associated with acid hypersecretion.

REFERENCE

Jensen RT. Gastrointestinal abnormalities and

involvement in systemic mastocytosis. *Hematol Oncol Clin North Am.* 2000;14(3):579-623. doi:10.1016/s0889-8588(05)70298-7

Question 36

A 75-year-old woman is referred to see you in clinic for evaluation of B12 deficiency. As part of her evaluation, her serum gastrin level is checked and found to be 1100 pg/mL (reference range, <100 pg/mL). She denies taking a proton pump inhibitor and has never had a history of peptic ulcer disease. What is the most likely diagnosis?

- A. *Helicobacter pylori* infection
- B. Pernicious anemia
- C. Surreptitious proton pump inhibitor use
- D. Zollinger-Ellison syndrome

CORRECT ANSWER: B

RATIONALE

Gastrin can be elevated for many reasons and can be classified as an appropriate or inappropriate elevation. In the case of pernicious anemia related to autoimmune atrophic gastritis, the parietal cell function is lost and achlorhydria develops in conjunction with loss of intrinsic factor. The loss of intrinsic factor and presence of achlorhydria would both lead to B12 deficiency, and the achlorhydria itself would lead to elevated gastrin, as this will increase in response to a lack of acid. *Helicobacter pylori* infection can increase gastrin but usually not to the level observed in this case. Surreptitious proton pump inhibitor use and Zollinger-Ellison syndrome would be possible, but much less likely if she has no history of peptic ulcer disease and denies taking a proton pump inhibitor.

REFERENCE

Murugesan SV, Varro A, Pritchard DM. Review article: Strategies to determine whether hypergastrinaemia is due to Zollinger-Ellison syndrome rather than a more common benign cause. *Aliment Pharmacol Ther.* 2009;29(10):1055-1068. doi:10.1111/j.1365-2036.2009.03976.x

Question 37

A 40-year-old man is referred to you for abdominal pain and diarrhea. Endoscopy shows a duodenal ulcer, and he is started on omeprazole 40 mg twice daily, with resolution of symptoms. The serum gastrin level is checked and found to be 780 pg/mL (reference range, <100 pg/mL). What is the most appropriate next step?

- A. Measure gastric pH during endoscopy
- B. Order cross-sectional abdominal imaging
- C. Perform a secretin stimulation test
- D. Stop omeprazole and recheck serum gastrin

CORRECT ANSWER: D

RATIONALE

This patient has an elevated serum gastric level in the context of a duodenal ulcer and diarrhea. Zollinger-Ellison syndrome is certainly on the differential diagnosis given these symptoms and findings; however, the serum gastrin level may also be elevated appropriately as a result of proton pump inhibitor (PPI)-induced acid suppression. The next step in evaluation would be to carefully stop the PPI (by tapering off) and repeat the gastrin measurement off PPI therapy to determine if it was a true elevation or simply spurious in the context of appropriate acid suppression. The other answer options would all be appropriate next steps in the evaluation of elevated gastrin and suspected Zollinger-Ellison syndrome if the repeat gastrin level off PPI therapy remained elevated.

REFERENCE

Murugesan SV, Varro A, Pritchard DM. Review article: Strategies to determine whether hypergastrinaemia is due to Zollinger-Ellison syndrome rather than a more common benign cause. *Aliment Pharmacol Ther.* 2009;29(10):1055-1068. doi:10.1111/j.1365-2036.2009.03976.x

Question 38

A 63-year-old woman from Mexico presents to your clinic with abdominal pain and weight loss. Evalua-

tion reveals *Helicobacter pylori* (*H pylori*) infection, and she is treated with quadruple therapy for a 2-week period. She feels well thereafter and stops all medications. You see her back in clinic 6 weeks later at which point she feels well with no symptoms. She would like to do a test to ensure that *H pylori* is eradicated. Which test would be the best option as a test of cure in this case?

- A. Endoscopy with biopsy
- B. Serology
- C. Stool antigen
- D. Stool culture

CORRECT ANSWER: C

RATIONALE

Serology for *H pylori* can detect prior exposure to the bacteria but not active infection/colonization. As such, it will remain positive after effective treatment and cannot be used as a test of cure. Stool antigen and urease breath testing would be the preferred options for confirmation of eradication, and both are sensitive when performed off proton pump inhibitor therapy. Endoscopy with biopsy is more invasive and expensive, less sensitive than either urease breath testing or stool antigen testing, and unnecessary in the absence of symptoms.

REFERENCES

El-Serag HB, Kao JY, Kanwal F, et al. Houston Consensus Conference on Testing for *Helicobacter pylori* Infection in the United States. *Clin Gastroenterol Hepatol*. 2018;16(7):992-1002.e6. doi:10.1016/j.cgh.2018.03.013

Fallone CA, Chiba N, van Zanten SV, et al. The Toronto Consensus for the Treatment of *Helicobacter pylori* Infection in Adults. *Gastroenterology*. 2016;151(1):51-69.e14. doi:10.1053/j.gastro.2016.04.006

Question 39

A 61-year-old man presents to the clinic for consultation regarding optimal gastrointestinal (GI)

management in the context of chronic ibuprofen use, which he requires for severe, unrelenting back pain. He has never had a history of peptic ulcer disease and denies any current GI symptoms. He has a history of a prior transient ischemic attack requiring anticoagulation, moderate alcohol use, and depression treated with amitriptyline. Which of the following is his biggest risk factor for future nonsteroidal antiinflammatory drug (NSAID)-induced GI bleeding?

- A. Age greater than 60 years
- B. Consumption of alcohol
- C. Need for anticoagulation
- D. Treatment with tricyclic antidepressant

CORRECT ANSWER: C

RATIONALE

Risk factors for NSAID-induced GI bleeding include age greater than 65 years, prior history of peptic ulcer disease or GI hemorrhage, and concomitant anticoagulation drug use. Moderate alcohol use and tricyclic antidepressant use are not considered significant risk factors.

REFERENCE

Lanas A, Chan FKL. Peptic ulcer disease. *Lancet*. 2017;390(10094):613-624. doi:10.1016/S0140-6736(16)32404-7

Question 40

A 50-year-old woman presents to the clinic with abdominal pain, nausea, and melena. She has no significant past medical history and takes no prescription medications, although she does take low-dose aspirin daily for prophylaxis. Evaluation reveals significant erosive gastropathy, and testing for *Helicobacter pylori* infection is negative. What is the most appropriate next step?

- A. Add omeprazole once daily
- B. Change aspirin to an enteric-coated formulation
- C. Continue low-dose aspirin
- D. Stop aspirin

CORRECT ANSWER: D

RATIONALE

If aspirin is taken for primary prevention and aspirin-associated bleeding occurs, antiplatelet therapy should be discontinued unless the patient is at high risk of cardiovascular complications. If aspirin is taken for secondary prevention, then a daily proton pump inhibitor should be added, and aspirin should be continued if the benefits are believed to justify the potential risks. In this case, as the patient is healthy and taking aspirin only for primary prophylaxis, the most reasonable option would be to discontinue it rather than add another medication to her regimen. Changing to an enteric-coated formulation sounds appealing, but there are no data showing this prevents GI complications. Likewise, continuing aspirin without change would not be an ideal option in the context of GI symptoms and bleeding.

REFERENCE

Laine L, Jensen DM. Management of patients with ulcer bleeding. *Am J Gastroenterol*. 2012;107(3):345-361. doi:10.1038/ajg.2011.480

Question 41

A 25-year-old woman with no past medical history presents to the clinic with postprandial abdominal pain that has been persistent despite unremarkable evaluation. Evaluation for *Helicobacter pylori* infection is negative, and she notes no improvement with daily proton pump inhibitors. What would be the most appropriate next step?

- A. Amitriptyline trial
- B. Antroduodenal manometry
- C. Metoclopramide trial
- D. Small intestinal bacterial overgrowth test

CORRECT ANSWER: B

RATIONALE

This patient has a classic presentation of functional dyspepsia or non-ulcer dyspepsia. As per

current guidelines, *Helicobacter pylori* infection should be evaluated for and treated if positive, and a trial of proton pump inhibitor therapy is recommended, as a minority of patients will have symptom improvement in this context. However, if there are no alarm findings, then symptom-based treatment is the most appropriate next step. Tricyclic antidepressants are often recommended as the next step, and a multicenter study has shown a benefit in this population with amitriptyline specifically. Antroduodenal manometry and small intestinal bacterial overgrowth testing would not be recommended in this context, and metoclopramide would not be recommended in the absence of nausea or impaired gastric emptying.

REFERENCES

Stanghellini V, Chan FK, Hasler WL, et al. Gastrointestinal Disorders. *Gastroenterology*. 2016;150(6):1380-1392. doi:10.1053/j.gastro.2016.02.011

Talley NJ, Locke GR, Saito YA, et al. Effect of Amitriptyline and Escitalopram on Functional Dyspepsia: A Multicenter, Randomized Controlled Study. *Gastroenterology*. 2015;149(2):340-9.e2. doi:10.1053/j.gastro.2015.04.020

Question 42

A 65-year-old patient with longstanding type 2 diabetes mellitus complicated by neuropathy and retinopathy presents to the clinic for evaluation of progressive early satiety, lack of appetite, nausea, and weight loss. What is the most appropriate next step?

- A. Gastric scintigraphy
- B. *Helicobacter pylori* test
- C. Omeprazole trial
- D. Upper endoscopy

CORRECT ANSWER: D

RATIONALE

This patient is elderly with several alarm findings

including weight loss. Although diabetic gastroparesis certainly is high on the differential diagnosis, endoscopy is a critical first step to exclude neoplasm, peptic ulcer disease, gastric outlet obstruction, or other mucosal findings before evaluating for less ominous diagnoses. In this situation, neither *Helicobacter pylori* testing, nor empiric medication trials would be appropriate given the alarm findings—unless pursued as a bridge before endoscopy can logistically be arranged.

REFERENCE

Stanghellini V, Chan FK, Hasler WL, et al. Gastroduodenal Disorders. *Gastroenterology*. 2016;150(6):1380-1392. doi:10.1053/j.gastro.2016.02.011

Question 43

A 65-year-old woman presents to the clinic for follow-up of abdominal pain in the context of a prior gastric ulcer. She has recently had a hip injury and needs to be on nonsteroidal antiinflammatory drugs (NSAIDs) for at least the next few months. She is worried that she might develop another gastric ulcer but is also terrified regarding potential side effects with proton pump inhibitors (PPIs). She asks you if there are any other options approved by the US Food and Drug Administration (FDA) for prevention of NSAID-associated gastrointestinal complications. Which medication do you suggest?

- A. Famotidine
- B. Misoprostol
- C. Sodium alginate
- D. Sucralfate

CORRECT ANSWER: B

RATIONALE

Misoprostol is a synthetic prostaglandin analogue that reduces gastric and duodenal NSAID-related ulceration and is FDA-approved for prophylaxis against NSAID-related gastrointestinal complications. It is not as effective as PPI therapy and can be associated with side effects including diarrhea;

however, it is an appropriate option in this situation if the patient needs to take an NSAID and is resistant to the idea of taking a PPI. Famotidine and other H₂ receptor antagonists are ineffective at preventing NSAID induced ulcerations, as are alginates and sucralfate.

REFERENCES

Lanza FL, Chan FK, Quigley EM; Practice Parameters Committee of the American College of Gastroenterology. Guidelines for prevention of NSAID-related ulcer complications. *Am J Gastroenterol*. 2009;104(3):728-738. doi:10.1038/ajg.2009.115

Yuan JQ, Tsoi KK, Yang M, et al. Systematic review with network meta-analysis: comparative effectiveness and safety of strategies for preventing NSAID-associated gastrointestinal toxicity. *Aliment Pharmacol Ther*. 2016;43(12):1262-1275. doi:10.1111/apt.13642

Question 44

A 55-year-old woman with systemic sclerosis on long-term immunosuppression and longstanding reflux on daily famotidine presents to the clinic with paresthesias in her hands and feet, an unsteady gait, and some recent memory changes. Additional analysis suggests B12 deficiency. Which of the following conditions is the most likely potential cause?

- A. Longstanding famotidine use
- B. Long-term immunosuppression
- C. Pancreatic exocrine insufficiency
- D. Small intestinal bacterial overgrowth

CORRECT ANSWER: D

RATIONALE

Vitamin B12 malabsorption can result from a variety of causes, but is often linked with autoimmune gastritis, longstanding proton pump inhibitor use, pancreatic exocrine insufficiency, small intestinal bacterial overgrowth (SIBO), or terminal ileum resection. In this case, the patient is taking famotidine instead of a proton pump inhibitor,

which is not believed to carry the same risk of B12 deficiency, presumably because the degree of acid suppression is far less with histamine-receptor blockade due to tachyphylaxis. Long-term immunosuppression is not a risk factor for B12 malabsorption per se, other than being a risk factor for SIBO. Both SIBO and pancreatic exocrine insufficiency would be conditions that can cause B12 deficiency; however, SIBO would be more likely in this context (systemic sclerosis, long-term immunosuppression, acid suppressive therapy).

REFERENCE

Stabler SP. Clinical practice. Vitamin B12 deficiency. *N Engl J Med*. 2013;368(2):149-160. doi:10.1056/NEJMc1113996

Question 45

A 72-year-old man with a recent myocardial infarction undergoes coronary angioplasty with stent placement and is started on aspirin and clopidogrel. He unfortunately develops transient melena in this context and presents to you for consultation about appropriate next steps. His melena has resolved, and he has no symptoms at the time of your visit. His primary care provider had mentioned the possibility of proton pump inhibitor (PPI) therapy, but he is very worried about potential side effects from PPI use as well as the potential for a PPI to affect the efficacy of his cardiac regimen. Which of the following would you add to his current treatment regimen?

- A. Famotidine
- B. Pantoprazole
- C. Omeprazole
- D. Sucralfate

ANSWER: B

RATIONALE

The patient in this case has both high cardiovascular risk (recent myocardial infarction and stent placement) and high gastrointestinal bleeding risk (recent melena). Given this, his best options

would be to add a PPI to his current regimen and continue his current cardiovascular medications if they are believed to be necessary. Famotidine has not been shown to be as effective as a PPI in this context. Regarding the potential for interactions between PPI use and clopidogrel, this has not been shown in systematic reviews of multiple trials; however, the strongest in vitro interactions have been with omeprazole and lansoprazole, so choosing another PPI (pantoprazole, rabeprazole) would be the best option. Sucralfate has not been shown to prevent ulceration in the setting of dual anti-platelet therapy.

REFERENCES

- Focks JJ, Brouwer MA, van Oijen MG, Lanan A, Bhatt DL, Verheugt FW. Concomitant use of clopidogrel and proton pump inhibitors: impact on platelet function and clinical outcome- a systematic review. *Heart*. 2013;99(8):520-527. doi:10.1136/heartjnl-2012-302371
- Lanas A, Chan FKL. Peptic ulcer disease. *Lancet*. 2017;390(10094):613-624. doi:10.1016/S0140-6736(16)32404-7

Question 46

A 23-year-old medical student interested in a potential career in infectious disease comes to see you in the clinic with postprandial abdominal pain. He is otherwise healthy and has had no prior gastrointestinal evaluation. You order a serum *Helicobacter pylori* (*H pylori*) antibody test, which comes back positive. You discuss the pros and cons of treatment, and he agrees to undergo eradication therapy; however, he asks you to consider published resistance patterns of *Helicobacter pylori* in your decision regarding antibiotic choice. Which antibiotic has the highest rate of *H pylori* resistance according to current evidence?

- A. Amoxicillin
- B. Clarithromycin
- C. Rifabutin
- D. Tetracycline

CORRECT ANSWER: B**RATIONALE**

Published data on *H pylori* sensitivity data suggest high rates of resistance to clarithromycin and metronidazole and emerging resistance to fluoroquinolones; however, currently, the other antibiotics listed in the answer choices are not believed to have resistance rates that are as high as those already mentioned. For this reason, clarithromycin would be the antibiotic to particularly avoid in this list if only antibiotics with low published resistance rates were to be pursued.

REFERENCE

Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection [published correction appears in *Am J Gastroenterol*. 2018 Jul;113(7):1102]. *Am J Gastroenterol*. 2017;112(2):212-239. doi:10.1038/ajg.2016.563

Question 47

A 58-year-old man presents with abdominal pain and melena. Evaluation shows erosive gastritis, and he is found to have *Helicobacter pylori* (*H pylori*) infection on gastric biopsy. He is treated appropriately with resolution of symptoms and presents for follow-up 12 weeks later. He is now off acid suppressive therapy and would like to pursue the single most sensitive test to ensure that he has cleared the *H pylori* infection. Which of the following tests would you recommend?

- A. Endoscopy with biopsies
- B. Serology
- C. Stool antigen evaluation
- D. Urease breath test

CORRECT ANSWER: D**RATIONALE**

The urease breath test and stool antigen test for *H pylori* are both believed to be greater than 95% sensitive for detection of active infection, assum-

ing patients are not on acid suppressive therapy at the time of testing. However, according to a recent Cochrane review and expert opinion, the breath test appears to be slightly more sensitive than the stool antigen test. Endoscopy is specific but less sensitive than both the breath test and stool antigen test. Serology is insensitive and has no role in eradication surveillance.

REFERENCE

Best LM, Takwoingi Y, Siddique S, et al. Non-invasive diagnostic tests for *Helicobacter pylori* infection. *Cochrane Database Syst Rev*. 2018;3(3):CD012080. Published 2018 Mar 15. doi:10.1002/14651858.CD012080.pub2

Question 48

A 62-year-old woman with Barrett's esophagus and prior erosive esophagitis responsive to proton pump inhibitor use presents to the clinic. She has been on lansoprazole for more than 15 years and is worried about potential long-term malabsorption.

Which of the following deficiencies is she at risk of developing?

- A. Folate
- B. Iron
- C. Vitamin E
- D. Vitamin K

CORRECT ANSWER: B**RATIONALE**

Long-term acid suppression from proton pump inhibitor (PPI) use has been linked to deficiencies in several vitamins and minerals including iron, B12, magnesium, and insoluble calcium. According to current evidence, long-term acid suppression has not been linked to deficiencies in folate, vitamin E, or vitamin K.

Although iron deficiency is not common with long-term PPI use, it can occur and has been reported to improve upon cessation of PPI therapy.

REFERENCE

Vaezi MF, Yang YX, Howden CW. Complications of Proton Pump Inhibitor Therapy. *Gastroenterology*. 2017;153(1):35-48. doi:10.1053/j.gastro.2017.04.047

Question 49

A 38-year-old man with a body mass index of 50 kg/m² presents to the bariatric clinic for evaluation of obesity. He has a history of hypertension, osteoarthritis, and asthma and is an active cigarette smoker and beer drinker. He also has a history of prior *Helicobacter pylori* infection, which was treated with proven eradication. He is very interested in undergoing Roux-en-Y gastric bypass surgery.

What is the single best step he can take to reduce his risk of potential anastomotic ulcers after surgery?

- A. Alcohol cessation
- B. Smoking cessation
- C. Stress reduction
- D. Strict dietary restriction

CORRECT ANSWER: B

RATIONALE

Marginal ulcers can be seen after Roux-en-Y gastric bypass and are believed to be related to local ischemia and the effects of gastric contents on intestinal mucosa. Risk factors include smoking, *Helicobacter pylori* infection, and nonsteroidal anti-inflammatory drug use.

In this example, smoking is the main modifiable risk factor identified and the correct choice.

REFERENCE

Wilson JA, Romagnuolo J, Byrne TK, Morgan K, Wilson FA. Predictors of endoscopic findings after Roux-en-Y gastric bypass. *Am J Gastroenterol*. 2006;101(10):2194-2199. doi:10.1111/j.1572-0241.2006.00770.x

Question 50

A 28-year-old man with occasional reflux symptoms presents to the clinic. He has symptoms of pyrosis only once to twice weekly at most. He is interested in a therapy that will work relatively quickly and can be taken on an intermittent basis only. He has tried calcium carbonate and aluminum hydroxide but has found both to be too short-acting. He has no alarm findings and does not desire endoscopy.

What therapy would be most ideal for this patient?

- A. Famotidine
- B. Rabeprazole
- C. Sucralfate
- D. Vonoprazan

CORRECT ANSWER: A

RATIONALE

This patient is an excellent candidate for a histamine-receptor blocker. These agents block gastric acid production by suppressing histamine release and work relatively quickly. They have tachyphylaxis with long-term use and thus are not ideal for indefinite daily therapy; however, they work relatively well on an intermittent basis and have an excellent cost/safety profile. Proton pump inhibitors such as rabeprazole are the most potent acid suppressive therapies on the market today in the United States, but they are much slower to act than histamine-receptor blockers and do not work as well for intermittent, on-demand use. Sucralfate is an aluminum salt that may inhibit pepsin activity in gastric fluid but is not as effective at acid suppression. Vonoprazan is a potassium competitive acid blocker that also affects the proton pump, but it is not approved in the United States currently.

REFERENCE

Kim J, Blackett JW, Jodorkovsky D. Strategies for Effective Discontinuation of Proton Pump Inhibitors. *Curr Gastroenterol Rep*. 2018;20(6):27. Published 2018 May 16. doi:10.1007/s11894-018-0632-y

CHAPTER 3

Pancreatic physiology & disease

Darshan Kothari, MD and Aparna Repaka, MD

Question 1

A 24-year-old woman with Down's syndrome presents to an emergency department physician with abdominal pain, nausea, postprandial fullness, and weight loss. Computed tomography is performed showing a distended stomach concerning for gastric outlet obstruction. The patient is admitted and has a nasogastric tube placed for decompression. An upper endoscopy is performed demonstrating extrinsic compression at the second part of the duodenum.

What is the most likely cause of her underlying obstruction?

- A. Autosomal dominant mutation in PRSS1 gene
- B. Fusion failure of ventral and dorsal duct systems
- C. Incomplete rotation of ventral and dorsal buds
- D. Intraduodenal dilation of common bile duct
- E. Recurrent gallstone obstruction at ampulla

CORRECT ANSWER: C**RATIONALE**

This patient with Down's syndrome has annular pancreas with pathophysiology that is best summarized as incomplete rotation of the ventral and dorsal buds. Autosomal dominant mutation in the *PRSS1* (serine protease 1) gene and recurrent gallstone obstruction at the ampulla present causes for recurrent acute pancreatitis that do not

typically present with duodenal obstruction. Fusion failure of the ventral and dorsal duct systems describes pancreatic divisum, which does represent a congenital abnormality of the pancreas but does not present with duodenal obstruction. Intraduodenal dilation of the common bile duct describes a type III choledochal cyst, which can present with duodenal obstruction but is not typically associated with Down's syndrome.

REFERENCE

Kozu T, Suda K, Toki F. Pancreatic development and anatomical variation. *Gastrointest Endosc Clin N Am.* 1995;5(1):1-30.

Question 2

A 7-year-old boy with a history of recurrent sinus infections presents to his pediatrician with abdominal pain and bloating. He was adopted at birth with no family history on file. On examination, the child ranges in the fourth percentile for both height and weight and has mild abdominal distension and digital clubbing.

What is the most likely underlying cause of his symptoms?

- A. Gastrin secreting neuroendocrine tumor
- B. Homozygous mutation in *CFTR* gene
- C. Marked elevated tissue transglutaminase
- D. Multiple small intestinal diverticula
- E. Transmural inflammation of terminal ileum

CORRECT ANSWER: B

RATIONALE

This child has a severe mutation in the *CFTR* (cystic fibrosis transmembrane conductance regular) gene resulting in severe pancreatic insufficiency. The CFTR protein plays a critical role in bicarbonate secretion from pancreatic ductal cells into the lumen, which is needed to neutralize gastric acid. Below a pH of 4, pancreatic enzymes are irreversibly inactivated.

The remaining choices all can cause pancreatic insufficiency but would be far less common in a 7-year-old patient.

REFERENCE

Ahmed N, Corey M, Forstner G, et al. Molecular consequences of cystic fibrosis transmembrane regulator (CFTR) gene mutations in the exocrine pancreas. *Gut*. 2003;52(8):1159-1164. doi:10.1136/gut.52.8.1159

Question 3

A 75-year-old man presents to an emergency department provider with painless jaundice, nausea, and progressive weight loss. Examination reveals a cachectic, jaundiced man with mild tenderness in the epigastrium. Computed tomography is performed showing a 3.4 cm mass in the head of the pancreas and compression of the common bile duct. The patient undergoes endoscopic retrograde cholangiopancreatography with placement of the metal stent and an endoscopic ultrasound with fine-needle aspiration that demonstrates pancreatic adenocarcinoma. Further work-up shows no metastatic disease. The patient undergoes a Whipple's procedure; however, 90% of the gland is ultimately removed. Pathology shows no nodal disease. Postoperatively, he continues to lose weight with upper abdominal bloating.

What is the next best step in management?

- A. Computed tomography
- B. Fecal elastase measurement
- C. Nutrition consultation

- D. Serum tumor marker measurement
- E. Upper endoscopy

CORRECT ANSWER: B

RATIONALE

The patient underwent a Whipple's procedure with 90% of his pancreas removed, which likely resulted in exocrine pancreatic insufficiency (EPI) as the pancreas no longer has reserves for enzyme production. Thus, fecal elastase measurement would be appropriate to assess EPI. Although the patient could have recurrence, it is unlikely given the negative work-up for metastatic disease; thus, assessment with computed tomography or serum tumor marker measurement this close after surgery is not indicated. Nutritional assessment may be key in helping the patient adjust to his new life, but this would be far more useful after establishing a diagnosis of EPI. Other causes for his abdominal pain and bloating may be possible but should be considered after assessment for EPI; thus, upper endoscopy is not indicated at this time.

REFERENCE

DiMagno EP, Go VL, Summerskill WH. Relations between pancreatic enzyme outputs and malabsorption in severe pancreatic insufficiency. *N Engl J Med*. 1973;288(16):813-815. doi:10.1056/NEJM197304192881603

Question 4

A 31-year-old man presents to a gastroenterologist with episodic epigastric abdominal pain, nausea, and vomiting. He has a history of recurrent acute pancreatitis since the age of 19 years, which was attributed to binge alcohol use while in college. Recently, his 2 younger siblings have also been diagnosed with acute pancreatitis. The patient undergoes magnetic resonance imaging, which shows evidence of chronic pancreatitis with pancreatic duct beading and gland atrophy.

Which of the following most accurately describes the etiology of his acute pancreatitis episodes?

- A. Gain-of-function mutation in *PRSS1* gene
- B. Homozygous mutation in *CFTR* gene
- C. Incomplete fusion of dorsal and ventral pancreatic ducts
- D. Incomplete rotation and fusion of ventral and dorsal buds
- E. Loss-of-function mutation in *SPINK1* gene

CORRECT ANSWER: A

RATIONALE

This patient has a form of hereditary pancreatitis from an autosomal dominant gain-of-function mutation in the *PRSS1* (serine protease 1) gene, which results in persistent activation of trypsin and subsequent autodigestion of the pancreatic gland and recurrence of acute pancreatitis. The patient's family history differentiates this form of hereditary pancreatitis from other forms such as those associated with *CFTR* (cystic fibrosis transmembrane conductance regular) or *SPINK1* (serine protease inhibitor Kazal-type 1) gene mutations. This patient also had imaging that ruled out congenital abnormalities such as pancreatic divisum, represented by incomplete fusion of the dorsal and ventral pancreatic ducts, and annular pancreas, represented by incomplete rotation and fusion of the ventral and dorsal buds.

REFERENCE

Whitcomb DC. Genetic aspects of pancreatitis. *Annu Rev Med.* 2010;61:413-424. doi:10.1146/annurev.med.041608.121416

Question 5

A 41-year-old woman presents to a gastroenterologist for a second opinion for her chronic abdominal pain. She reports constant, dull epigastric pain that worsens within 30 minutes of eating and is associated with ingestion of fatty foods. She underwent upper endoscopy, computed tomography, and magnetic resonance cholangiopancreatography, all of which were normal. She recently had an endoscopic ultrasound showing side branch dilations, hyperechoic foci without

acoustic shadowing, and lobularity without honeycomb pattern.

Which of the following is the best test for diagnosing this patient's condition?

- A. Diagnostic endoscopic retrograde pancreatography
- B. Duodenal bicarbonate concentration after intravenous secretin injection
- C. Endoscopic ultrasound with intravenous secretin injection
- D. Fecal elastase concentration after enzyme supplementation
- E. Postprandial serum lipase and amylase levels

CORRECT ANSWER: B

RATIONALE

This patient presents with symptoms that may be suggestive of chronic pancreatitis without overt radiographic findings and indeterminate findings on endoscopic ultrasound. Pancreatic function testing with secretin can assess pancreatic ductal function by measuring duodenal concentrations of bicarbonate after intravenous administration of secretin. Although subtle ductal changes may be seen on diagnostic endoscopic retrograde pancreatography (ERCP), the risk of post-ERCP pancreatitis outweigh the benefits in most cases and should not be pursued in this patient. Endoscopic ultrasound with intravenous secretin injection, fecal elastase concentration after enzyme supplementation, and postprandial serum lipase and amylase levels do not provide function testing.

REFERENCE

Ketwaroo GA, Freedman SD, Sheth SG. Approach to patients with suspected chronic pancreatitis: a comprehensive review. *Pancreas.* 2015;44(2):173-180. doi:10.1097/MPA.0000000000000239

Question 6

A 66-year-old man with longstanding type 1 diabe-

tes complicated by peripheral neuropathy presents to this primary care with a 3-month history of progressive weight loss, postprandial bloating, and steatorrhea. His medications include gabapentin and both long- and short-acting insulin. He denies prior abdominal surgery. Examination and laboratory tests are unrevealing except for a hemoglobin A_{1c} of 8.9% (reference range, 4.0%-5.6%). A computed tomography scan shows no abnormalities other than mild pancreatic atrophy.

Which of the following is the next best step in managing his new symptoms?

- A. Fecal elastase measurement
- B. Hydrogen breath testing
- C. Insulin dose adjustment
- D. Nutritional assessment
- E. Serum tissue transglutaminase measurement

CORRECT ANSWER: A

RATIONALE

This patient is exhibiting signs of exocrine pancreatic insufficiency (EPI). Given his longstanding history of diabetes with poor control, an assessment for EPI (fecal elastase measurement) is the most appropriate step. Islet hormones may affect both acinar cell digestive enzyme content and secretion. One effect of this relationship might be the relative pancreatic exocrine insufficiency observed in diabetics as seen in this case. If the fecal testing is normal, it would be reasonable to assess for small intestinal bacterial overgrowth (hydrogen breath testing) and celiac disease (serum tissue transglutaminase measurement). Certainly, insulin adjustment is needed in this case given his hemoglobin A_{1c} result; however, insulin dose

adjustment is unlikely to address his new symptoms. Lastly, although nutritional assessment may be useful in understanding his symptoms, it would be a better choice after establishing a diagnosis of EPI.

REFERENCE

Radlinger B, Ramoser G, Kaser S. Exocrine Pancreatic Insufficiency in Type 1 and Type 2 Diabetes. *Curr Diab Rep.* 2020;20(6):18. Published 2020 Apr 1. doi:10.1007/s11892-020-01304-0

Question 7

A 45-year-old woman presents to an emergency department provider with acute-onset epigastric pain, nausea, and vomiting. She has no past medical history and does not take any medications. She is in moderate distress from her pain and has the following vital signs: temperature, 37.6°C; heart rate, 123 bpm; blood pressure, 102/62 mmHg; respiratory rate, 14 breaths per minute; and oxygen saturation, 97% on room air. Her examination is notable for tenderness in the upper abdomen without rebound or guarding.

Laboratory evaluation is shown below.

The patient undergoes a computed tomography scan showing diffuse peripancreatic stranding and is diagnosed with acute pancreatitis. She is admitted to the general medicine ward where she receives intravenous fluids and analgesia. She reports current tobacco use of 1 pack daily and drinks 1 to 2 alcoholic beverages weekly. She denies illicit drug use.

Which of the following tests should be part of her inpatient workup?

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	150	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	84	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	38	10-40
Bilirubin, total, serum, mg/dL	0.9	0.3-1.0
Leukocyte (WBC) count, cells/ μ L	12,000	4000-11,000
Lipase, serum, U/L	11,000	10-140

- A. *CFTR* mutation analysis
- B. Chemical dependency assessment
- C. Magnetic resonance cholangiopancreatography
- D. Right upper quadrant ultrasound
- E. Serum immunoglobulin G subclass measurement

CORRECT ANSWER: D

RATIONALE

In the United States, the most common cause of acute pancreatitis is gallstones; thus, this patient requires dedicated imaging. The most appropriate choice in this case would be a right upper quadrant ultrasound and not more advanced imaging such as magnetic resonance cholangiopancreatography. As this is the patient's first case of acute pancreatitis, it would not be appropriate to perform *CFTR* (cystic fibrosis transmembrane conductance regulator) mutation analysis. Although alcohol use is also a common cause of acute pancreatitis, typically this is associated with heavy use (5 drinks daily for 5 years), which is not the case with this patient; thus, chemical dependency assessment is not correct. Serum measurement for immunoglobulin G (IgG) subclasses would be appropriate if there were concern for IgG4-related acute pancreatitis, which typically presents in patients in their 60s and with obstructive jaundice, neither of which are true in this case.

REFERENCE

Forsmark ChE, Vege SS, Wilcox CM. Acute Pancreatitis. *N Engl J Med*. 2017;376(6):598-599. doi:10.1056/NEJMc1616177

Question 8

A 54-year-old man with a history of tobacco use and hypertension presents to his primary care provider after a recent hospitalization for his first episode of acute pancreatitis. He recalls experiencing acute-onset, severe abdominal pain, for which he presented to his local emergency department and was given a diagnosis of acute pancreatitis. His discharge summary reports that his course was uncomplicated, and he was discharged within 72 hours. While admitted, he had a right upper quadrant ultrasound, which showed no gallstones. He denied alcohol use. He now presents for follow-up where he now feels well but reports a 15-pound weight loss, which he attributes to his recent hospitalization. He takes lisinopril and vitamin D. Fasting laboratory tests at this visit are shown below.

What is the next best step in the management of this patient?

- A. Antihypertensive medication change
- B. Fecal elastase measurement
- C. Magnetic resonance imaging
- D. Serum immunoglobulin G subclass measurement
- E. Tobacco cessation counselling

CORRECT ANSWER: C

RATIONALE

This patient presents to his primary care provider after a single episode of acute pancreatitis without an etiology identified. Pancreatic cancer

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	165	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	45	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	37	10-40
Bilirubin, total, serum, mg/dL	0.8	0.3-1.0
Calcium, serum, mg/dL	8.4	8.6-10.2
Glucose, plasma (fasting), mg/dL	134	70-99
Hemoglobin, blood, g/dL	13.4	14-18
Leukocyte (WBC) count, cells/ μ L	9700	4000-11,000
Platelet count, plt/μ L	313,000	150,000-450,000
Triglycerides, serum (fasting), mg/dL	160	<150

infrequently presents as acute pancreatitis, and patients without a clear history of gallstones or alcohol use should undergo follow-up imaging to rule out space-occupying lesions, especially if they have any of the following risk factors: age greater than 40 years, cigarette smoking, weight loss, cholestatic liver injury, and glucose intolerance. In this case, this patient had several risk factors; thus, magnetic resonance imaging is the best answer. Although it is possible that lisinopril may be the causative factor, given his multiple risk factors, imaging is the most appropriate next step. If imaging is negative, a change in antihypertensive medication may be appropriate. As the patient has no evidence of steatorrhea or jaundice, evaluations for exocrine pancreatic insufficiency (fecal elastase measurement) or autoimmune pancreatitis (serum immunoglobulin G subclass measurement) are not indicated. Tobacco smoking increases the risk of both chronic pancreatitis and pancreatic cancer; however, it does not cause acute pancreatitis. Although tobacco cessation counseling is important to this patient’s overall health, it would not be the next best step in management.

REFERENCE

Dzeletovic I, Harrison ME, Crowell MD, et al. Pancreatitis before pancreatic cancer: clinical features and influence on outcome. *J Clin Gastroenterol*. 2014;48(9):801-805. doi:10.1097/MCG.0b013e3182a9f879

Question 9

A 42-year-old woman with history of celiac disease and hypothyroidism presents to an emergency department provider with 4 weeks of abdominal pain, nausea, and diarrhea that have progressively worsened over the last week. She denies weight loss, recent travel, and blood in the stool. She takes levothyroxine daily. She denies tobacco and alcohol use. In the emergency department, her vitals are stable, and she is nontoxic appearing. Her abdominal examination is notable for mild diffuse tenderness.

Laboratory results are below.

Computed tomography is performed, and a representative axial image is below. She is admitted for acute pancreatitis where she receives intravenous fluids and analgesia. Within 48 hours, her pain and nausea improve, and she is started on oral feeding.

While admitted, she has triglyceride and calcium tests performed, which are normal. A right upper quadrant ultrasound shows no cholelithiasis.

What is the next best step in management?

- A. Colonoscopy with colon and ileal biopsies
- B. Empiric course of steroids

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	215	30-120
Leukocyte (WBC) count, cells/ μ L	12,000	4000-11,000
Lipase, serum, U/L	234	10-140



- C. Endoscopic ultrasound with fine needle biopsy
- D. Serum measurement of immunoglobulin G subclasses
- E. Surgical consultation for laparoscopic biopsy and/or resection

CORRECT ANSWER: C

RATIONALE

This patient is presenting with a subacute course of abdominal pain and nausea with an elevated lipase level, pancreatic inflammatory changes on computed tomography, and a pancreatic mass in the context of other autoimmune diseases, all of which are suggestive of type 2 autoimmune pancreatitis. However, further evaluation with fine-needle biopsy is needed to confirm the diagnosis; without it, empiric treatment with steroids should not be employed. If fine needle biopsy were to not provide a definitive diagnosis, then surgical resection/biopsy can be considered. Autoimmune pancreatitis may be the underlying process; however, given her age and sex, type 2 autoimmune pancreatitis should be considered. It is not part of the immunoglobulin G4 (IgG4)-related disease spectrum; thus, measurement of serum IgG4 levels would not provide any additional diagnostic information. Type 2 autoimmune pancreatitis is however associated with inflammatory bowel disease. As this patient has had diarrhea, a colonoscopy with colon and ileal biopsies should be considered at some point. However, the initial effort should focus on diagnosis of the pancreatic mass.

REFERENCE

Majumder S, Takahashi N, Chari ST. Autoimmune Pancreatitis. *Dig Dis Sci*. 2017;62(7):1762-1769. doi:10.1007/s10620-017-4541-y

Question 10

A 48-year-old man with imaging showing a pancreatic mass undergoes an endoscopic ultrasound with fine-needle biopsy. Histology demonstrates

periductal lymphoplasmacytic infiltrate with edematous stroma and neutrophils in the ductal epithelium suggestive of idiopathic duct-centric pancreatitis. He is started on prednisone 40 mg for 1 month and has repeat computed tomography that shows near resolution of his previously noted mass lesion. He subsequently completes a steroid taper. Two months later, he presents to his gastroenterologist with recurrent abdominal pain, nausea, and diarrhea. He is restarted on steroids, which resolves the pain and nausea.

What is the next best step in the workup of this patient?

- A. Colonoscopy with colon and ileal biopsies
- B. Endoscopic ultrasound with possible fine-needle biopsy
- C. Fecal elastase measurement
- D. Magnetic resonance imaging with cholangiopancreatography
- E. Serum C-reactive protein measurement

CORRECT ANSWER: A

RATIONALE

This patient has an established diagnosis of idiopathic duct-centric pancreatitis (type 2 autoimmune pancreatitis) with pathognomonic findings of a granular epithelial lesion. Patients with type 2 autoimmune pancreatitis often have comorbid inflammatory bowel disease. As this patient presents with recurrent diarrhea, further workup with colonoscopy with colon and ileal biopsies is warranted to rule out inflammatory bowel disease. Given the established diagnosis of type 2 autoimmune pancreatitis and appropriate response to steroids, repeat imaging or endoscopic ultrasound are not necessary at this point. The patient has diarrhea with no other evidence of exocrine pancreatic insufficiency; as such, fecal elastase measurement is incorrect. Although C-reactive protein may be useful in the workup for inflammatory bowel disease, it will not provide definite diagnostic data.

REFERENCE

Tsen A, Alishahi Y, Rosenkranz L. Autoimmune Pancreatitis and Inflammatory Bowel Disease: An Updated Review. *J Clin Gastroenterol*. 2017;51(3):208-214. doi:10.1097/MCG.0000000000000737

Question 11

A 61-year-old woman with history of hypertension and diabetes complicated by end-stage renal failure now 4 weeks after kidney transplantation presents to her transplant nephrologist with 2 days of fevers, nausea, and abdominal pain. She received a cytomegalovirus-negative kidney. Her current medications include: lisinopril, amlodipine, metformin, insulin, prednisone, azathioprine, and tacrolimus. She is ill-appearing and directed to the emergency department where her initial vitals are: temperature, 38.0°C; blood pressure, 80/45 mmHg; heart rate, 132 bpm; respiratory rate, 20 breaths per minute; oxygen saturation, 91% on room air.

She is triaged to the resuscitation bay where she is noted to be confused and have diffuse abdominal discomfort. She receives intravenous fluids and undergoes laboratory evaluation demonstrating the following shown below. (Table A)

A chest radiograph demonstrates prominent pulmonary vasculature without pulmonary infiltrates and small bilateral pleural effusions. Computed tomography is performed with a pre-sentative coronal and axial image provided on the following page.

The patient receives additional fluids with repeat vital signs: temperature, 38.7°C; blood pressure, 101/46 mmHg; heart rate, 100 bpm; respiratory rate, 16 breaths per minute; and oxygen saturation, 97% on 2 L of oxygen by nasal canula. Repeat examination reveals improved mental status but continued diffuse abdominal tenderness.

Laboratory results are demonstrated on the following page. (Table B)

Table A

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	98	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	38	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	34	10-40
Bilirubin, total, serum, mg/dL	0.9	0.3-1.0
Blood urea nitrogen (BUN), serum or plasma, mg/dL	85	8-20
Calcium, serum, mg/dL	8.1	8.6-10.2
Carbon dioxide content, serum, mEq/L	12	23-30
Chloride, serum, mEq/L	102	98-106
Creatinine, serum, mg/dL	3.1 (baseline, 1.4)	0.7-1.5
Glucose, plasma (fasting), mg/dL	323	70-99
Hemoglobin, blood, g/dL	17	14-18
Lactic acid, serum, mmol/L	4.1	0.7-2.1
Leukocyte (WBC) count, cells/ μ L	23,000	4000-11,000
Lipase, serum, U/L	24,234	10-140
Platelet count, plt/ μ L	151,000	150,000-450,000
Potassium, serum, mEq/L	5.1	3.5-5.0
Sodium, serum, mEq/L	132	136-145

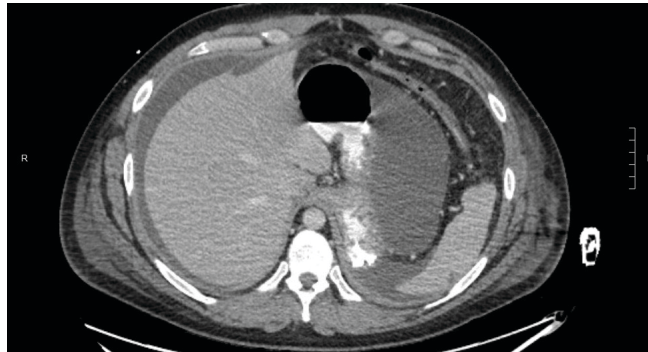
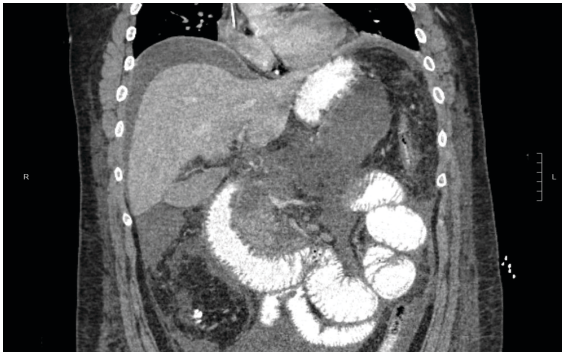


Table B

Laboratory Test	Result	Reference Range
Blood urea nitrogen (BUN), serum or plasma, mg/dL	71	8-20
Creatinine, serum, mg/dL	2.7 (baseline, 1.4)	0.7-1.5
Hemoglobin, blood, g/dL	14	14-18

In addition to ongoing fluid resuscitation, what is the next best step in management?

- Broad-spectrum antibiotics to treat infection
- Endoscopic retrograde cholangiopancreatography to treat pancreatic duct disruption
- Intensive care unit admission for close monitoring
- Percutaneous drainage of fluid collection
- Surgical consultation for cholecystectomy

CORRECT ANSWER: C

RATIONALE

This patient is presenting with acute pancreatitis with evidence of end-organ damage as documented by hypoxia and creatinine level above her baseline as well as evidence of systemic inflammatory response syndrome. By the revised Atlanta criteria, she would be classified as severe acute pancreatitis given her local complications as demonstrated on computed tomography. Furthermore, the BISAP (Bedside Index for Severity in Acute Pancreatitis) score is 5, which predicts a mortality of 22%. The 2018 American Gastroenterological Association (AGA) guidelines recommend close clinical monitoring for patients with severe acute

pancreatitis for these reasons; thus, admission to the intensive care unit is the best next step. Her fever and systemic inflammatory response are likely due to her severe acute pancreatitis. In the absence of documented infection or persistent hypotension, the AGA guidelines advise against empiric antibiotics. Furthermore, given that the patient is in her early course, percutaneous drainage and pancreatic duct stent is contraindicated. Lastly, as there is no evidence to support gallstones, cholecystectomy would not be indicated.

REFERENCES

Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102-111. doi:10.1136/gutjnl-2012-302779

Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN; American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. *Gastroenterology*. 2018;154(4):1096-1101. doi:10.1053/j.gastro.2018.01.032

Question 12

A-55 year-old woman who underwent kidney

transplantation is admitted for severe acute pancreatitis. While admitted, a right upper quadrant ultrasound is performed and is negative for cholelithiasis. On hospital day 7, she is discharged on enteral tube feeding with improvement in her symptoms and is instructed to return for close outpatient follow-up. At her follow-up appointment, the patient is feeling better and reports that 2 nights ago she accidentally pulled out her feeding tube. Since then, she has been tolerating an oral diet without any symptoms. Before hospital admission, the patient's immunosuppression regimen consisted of prednisone, azathioprine, and tacrolimus. At discharge, the patient was told to hold azathioprine until her follow-up.

What is the most appropriate recommendation regarding her azathioprine?

- A. Check serum thiopurine S-methyltransferase activity
- B. Check thiopurine metabolite levels
- C. Rechallenge at lower dose
- D. Switch to different drug class
- E. Switch to 6-mercaptopurine

CORRECT ANSWER: D

RATIONALE

The patient likely has azathioprine-induced acute pancreatitis. Thiopurine-induced pancreatitis is a dose-independent idiosyncratic reaction usually seen in the first month of therapy. Thiopurine S methyltransferase polymorphisms are not associated with risk and thus checking metabolites or enzyme activity would not be helpful. Although pancreatitis is usually clinically mild, thiopurine rechallenge is contraindicated. The correct answer is therefore to switch to a different drug class.

REFERENCE

van Geenen EJ, de Boer NK, Stassen P, et al. Azathioprine or mercaptopurine-induced acute pancreatitis is not a disease-specific phenomenon. *Aliment Pharmacol Ther*.

2010;31(12):1322-1329. doi:10.1111/j.1365-2036.2010.04287.x

Question 13

A 41-year-old woman with a history of obesity and depression presents with acute-onset abdominal pain and nausea that began 10 hours before presentation. She is currently on citalopram. She denies tobacco use and drinks 1 to 2 glasses of wine monthly. On arrival to the emergency department, her vital signs are: temperature, 36.8°C; blood pressure, 142/87 mmHg; heart rate, 92 bpm; respiratory rate, 14 breaths per minute; and oxygen saturation, 98% on room air. Examination is notable for epigastric tenderness. Her laboratory tests demonstrate normal complete blood count, electrolytes, and kidney function.

The remainder of her laboratory results are shown at the top of the following page.

A computed tomography scan is performed showing mild peripancreatic stranding around the head and uncinate process of the pancreas. She receives intravenous fluids and analgesia. She undergoes a right upper quadrant ultrasound, which shows small gallstones in her gallbladder without gallbladder wall thickening or fluid. Her common bile duct measured 5 mm (reference range, <6 mm). Four hours later, she reports significant improvement in symptoms and is now tolerating a full diet.

What is the next step in management?

- A. Consultation for cholecystectomy
- B. Discharge and follow-up with primary care provider
- C. Endoscopic ultrasound
- D. Liver function tests
- E. Magnetic resonance cholangiopancreatography

CORRECT ANSWER: A

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	198	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	104	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	64	10-40
Bilirubin, total, serum, mg/dL	0.8	0.3-1.0
Lipase, serum, U/L	1404	10-140

RATIONALE

This patient is presenting with mild acute pancreatitis secondary to gallstones. Randomized controlled trials demonstrate a benefit for same-admission cholecystectomy to reduce the risk of gallstone-related complications. As such, the American Gastroenterological Association has proposed hospital-based quality metrics, one of which includes cholecystectomy during the index admission for patients with gallstone pancreatitis. Thus, cholecystectomy consultation is the best answer. Although the patient has drastically improved in her short visit to the emergency department, it would not be appropriate to discharge her without evaluation for cholecystectomy. It would, however, be reasonable to discharge her if close follow-up with surgery can be arranged within 7 days of discharge. Although the patient does have abnormal liver tests, there is no evidence of choledocholithiasis. As such, further imaging by endoscopic ultrasound or magnetic resonance imaging is not indicated. Furthermore, work-up for abnormal liver tests can be considered if the patient has persistent liver test abnormalities after cholecystectomy.

REFERENCES

Ahmed A, Kothari DJ, Wardlaw S, Freedman SD, Sheth SG. Reducing Hospitalization in Mild Acute Pancreatitis: Results of Long-term Follow-up. *J Clin Gastroenterol*. 2021;55(2):180-186. doi:10.1097/MCG.0000000000001354

Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN; American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. *Gastroenterology*. 2018;154(4):1096-1101. doi:10.1053/j.gastro.2018.01.032

da Costa DW, Bouwense SA, Schepers NJ, et al. Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomised controlled trial. *Lancet*. 2015;386(10000):1261-1268. doi:10.1016/S0140-6736(15)00274-3

Question 14

A 38-year-old man presents with intermittent mild upper abdominal pain and an elevated lipase level. The patient previously reported upper abdominal pain to his primary care provider 4 months ago. At that time, laboratory tests were performed showing the following below.

The elevated lipase level prompted computed tomography and magnetic resonance imaging with cholangiopancreatography, both of which were normal. The patient was then referred to gastroenterology. He currently denies abdominal pain. He has chronic low back pain that is treated with codeine. He smokes tobacco daily and denies alcohol or illicit drug use. He denies a family history of pancreatic disease, and review of systems

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	98	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	39	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	34	10-40
Bilirubin, total, serum, mg/dL	0.9	0.3-1.0
Lipase, serum, U/L	201	10-140

is negative including weight loss, jaundice, nausea, and vomiting. He denies ever being told he had pancreatic issues. He is concerned about his elevation in lipase value especially because his neighbor just died of pancreatic cancer. What is the next best step in management?

- A. Measure immunoglobulin G subtypes
- B. Order secretin pancreatic function test
- C. Perform endoscopic ultrasound
- D. Provide reassurance with anticipatory guidance
- E. Repeat serum amylase and lipase tests

CORRECT ANSWER: D

RATIONALE

This case of hyperlipasemia in an otherwise asymptomatic patient is a common occurrence, which a practicing gastroenterologist will inevitably face. In this case, the patient had vague abdominal symptoms with a lipase elevation that was less than 2 times the upper limit of normal, neither of which were consistent with acute pancreatitis. Furthermore, 2 high-quality imaging tests were negative. Thus, pancreatic disease has been satisfactorily ruled out especially in the absence of gastrointestinal symptoms. In this case, the most likely cause of his elevated lipase level is codeine. Thus, reassurance with anticipatory guidance on red flag symptoms (ie, symptoms of acute pancreatitis, jaundice, and weight loss) would be the most appropriate step in management. The patient has no evidence of immunoglobulin G4-related disease; thus, measuring

serum immunoglobulin G subtypes is incorrect. Pursuing additional testing (secretin pancreatic function test, endoscopic ultrasound, and repeat serum amylase and lipase tests) would be excessive and unnecessarily costly.

REFERENCE

Gumaste VV, Roditis N, Mehta D, Dave PB. Serum lipase levels in nonpancreatic abdominal pain versus acute pancreatitis. *Am J Gastroenterol*. 1993;88(12):2051-2055.

Question 15

A 50-year-old man with a history of hyperlipidemia presents to an emergency department provider with acute-onset severe abdominal pain, nausea, and vomiting. The patient's medication list includes simvastatin. He denies tobacco or alcohol use and has no family history of pancreatic diseases. His initial vital signs are: temperature, 37.6°C; heart rate, 101 bpm; blood pressure, 100/46 mmHg; respiratory rate, 14 breaths per minute; oxygen saturation, 99% on room air. Examination reveals clear lungs and tenderness in the epigastric area.

Computed tomography is performed demonstrating diffuse peripancreatic stranding with an approximately 5.1 x 3.0 cm area of relative hypodensity in the mid/distal pancreatic tail suggestive of necrosis. The patient receives intravenous fluids and analgesia and is admitted to the general medicine service. Over the course of 72 hours, the patient's kidney function improves; however, he

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	102	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	40	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	19	10-40
Bilirubin, total, serum, mg/dL	0.7	0.3-1.0
Blood urea nitrogen (BUN), serum or plasma, mg/dL	31	8-20
Creatinine, serum, mg/dL	1.8 (baseline, 0.8)	0.7-1.5
Hemoglobin, blood, g/dL	14	14-18
Leukocyte (WBC) count, cells/ μ L	12,000	4000-11,000
Lipase, serum, U/L	2340	10-140

continues to complain of pain and nausea, which prevents him from eating. What is the next best step in management?

- A. Begin clear liquid diet and advance as tolerated
- B. Initiate total peripheral nutrition
- C. Place nasogastric tube for nutritional support
- D. Repeat cross-sectional imaging for interval findings
- E. Start broad-spectrum antibiotics

CORRECT ANSWER: C

RATIONALE

This patient presented with moderately severe acute pancreatitis with cross-sectional imaging suggestive of necrosis. Given his presentation and persistent symptoms, he is unlikely to improve within the next 7 days. Thus, nutritional support with nasogastric feedings is indicated. Although starting a clear liquid diet may be considered, it is unlikely to provide him with the nutritional support he needs. Several studies have demonstrated that the use of total parenteral nutrition should be avoided in patients with acute pancreatitis and would not be appropriate for this patient. The patient's persistence of symptoms is reflective of his moderately severe disease. In the absence of changes in clinical status (ie, new fever or clinical decompensation), repeat imaging and antibiotics are not indicated.

REFERENCES

Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN; American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. *Gastroenterology*. 2018;154(4):1096-1101. doi:10.1053/j.gastro.2018.01.032

Vaughn VM, Shuster D, Rogers MAM, et al. Early Versus Delayed Feeding in Patients With Acute Pancreatitis: A Systematic Review. *Ann Intern Med*. 2017;166(12):883-892. doi:10.7326/M16-2533

Question 16

A 73-year-old woman presents to the emergency department with abdominal pain and nausea. She has a history of osteoarthritis, breast cancer, and hypothyroidism. Her medications include levothyroxine, calcium, and vitamin D. She denies tobacco and alcohol use. Symptoms began suddenly 15 hours before presentation. On arrival to the emergency department, her vital signs are: temperature, 38.4°C; heart rate, 109 bpm; blood pressure, 110/76 mmHg; respiratory rate, 15 breaths per minute; and oxygen saturation, 99% on room air. Her examination demonstrates an ill-appearing female in moderate distress from pain with scleral icterus and diffuse abdominal tenderness. Laboratory results are below.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	398	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	254	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	234	10-40
Bilirubin, total, serum, mg/dL	4.1	0.3-1.0
Chloride, serum, mEq/L	101	98-106
Glucose, plasma (fasting), mg/dL	73	70-99
Hemoglobin, blood, g/dL	13	14-18
Leukocyte (WBC) count, cells/ μ L	21,000	4000-11,000
Lipase, serum, U/L	8767	10-140
Platelet count, plt/μ L	210,000	150,000-450,000
Potassium, serum, mEq/L	4.1	3.5-5.0
Sodium, serum, mEq/L	142	136-145

A right upper quadrant ultrasound is performed showing a distended gallbladder with mobile gallstones and a common bile duct measuring 1.1 cm. The patient receives intravenous fluids, antibiotics, and analgesia and is admitted to general medicine for further management. Overnight she develops a fever to 38.9°C and hypotension, which is responsive to fluids. She is transferred to the intensive care unit for close monitoring. Blood cultures grow Gram-negative rods.

In addition to critical care monitoring and resuscitation, what is next best step in management?

- A. Endoscopic retrograde cholangiopancreatography
- B. Endoscopic ultrasound
- C. Magnetic resonance imaging with cholangiopancreatography
- D. Percutaneous biliary decompression
- E. Urgent cholecystectomy consultation

CORRECT ANSWER: A

RATIONALE

The patient is presenting with acute gallstone pancreatitis, which is complicated by cholangitis and bacteremia. With progressive septic shock, source control is needed urgently; thus, urgent endoscopic drainage with endoscopic retrograde cholangiopancreatography (ERCP) is the correct answer. In this urgent case, repeat imaging with endoscopic ultrasound or magnetic resonance imaging would not be appropriate. If the patient were too sick to undergo endoscopy or had altered anatomy such that standard ERCP could not be performed, then percutaneous drainage can be considered. However, in this case, the patient should be considered for ERCP first and not percutaneous drainage. Lastly,

although cholecystectomy will be critical in reducing further complications from gallstones, urgent cholecystectomy is not indicated at this moment.

REFERENCE

Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN; American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. *Gastroenterology*. 2018;154(4):1096-1101. doi:10.1053/j.gastro.2018.01.032

Question 17

A 62-year-old man presents to the emergency department with acute-onset abdominal pain, nausea, and vomiting. He has a history of coronary disease, hypertension, anxiety, posttraumatic stress disorder, and depression. His medication list includes aspirin, ticagrelor, carvedilol, and escitalopram. He smokes 1 pack of cigarettes daily and reports social alcohol use. On arrival to the emergency department, his vital signs are: temperature, 36.6°C; blood pressure, 160/100 mmHg; heart rate, 110 bpm; respiratory rate, 14 breaths per minute; oxygen saturation, 96% on room air. Examination is notable for a tremulous male in mild distress from pain, anxiety, and tenderness in the upper abdomen. Laboratory results are notable for normal complete blood count, electrolytes, and kidney function.

The remainder of laboratory results are below.

Computed tomography is performed showing peripancreatic stranding around the head of the pancreas with scattered coarse calcifications throughout the pancreas and pancreatic duct ir-

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	179	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	98	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	234	10-40
Bilirubin, total, serum, mg/dL	1.6	0.3-1.0
Lipase, serum, U/L	3747	10-140

regularity. The patient is admitted and has a right upper quadrant ultrasound, which is negative for gallstones. He is managed conservatively with fluids and analgesia. By hospital day 2, his symptoms have improved, and he is eating a full diet. He requests discharge, stating that his landscaping business will suffer without him.

Before discharge, which of the following should be considered as part of his inpatient workup?

- A. Endoscopic ultrasound
- B. Magnetic resonance imaging with cholangiopancreatography
- C. *PRSS1*, *SPINK1*, *CTRC*, and *CFTR* mutation testing
- D. Serum immunoglobulin G subclass measurement
- E. Social work consultation

CORRECT ANSWER: E

RATIONALE

This patient is presenting with acute pancreatitis with imaging suggestive of underlying chronic pancreatitis. Additionally, he initially had evidence of tremulousness suggestive of alcohol withdrawal and elevated liver enzymes in a 2:1 pattern suggestive of mild alcoholic hepatitis. In this case, the most appropriate next step would be social work consultation to assess chemical dependency and provide resources on abstinence. Studies have demonstrated that inpatient alcohol counseling reduces subsequent episodes; thus, the American Gastroenterological Association guidelines recommend this for all patients with acute alcoholic pancreatitis. In this case, the patient's imaging suggests clear evidence of chronic pancreatitis, which may be contributing to his episode of acute pancreatitis. However, in the setting of his acute flare, endoscopic ultrasound and magnetic resonance imaging with cholangiopancreatography should not be used. Furthermore, he has clear evidence of alcohol-related disease; thus, assessment of genetic abnormalities and autoimmune pancreatitis are not appropriate.

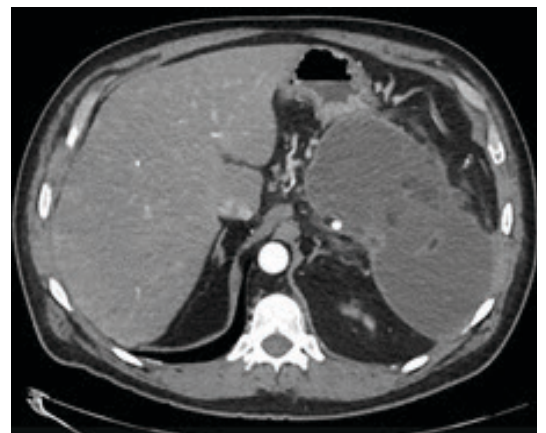
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Lappalainen-Lehto R, Koistinen N, Aalto M, et al. Goal-related outcome after acute alcohol-pancreatitis -- a two-year follow-up study. *Addict Behav*. 2013;38(12):2805-2809. doi:10.1016/j.addbeh.2013.07.008

Question 18

A 45-year-old woman is transferred from a community hospital to a tertiary center for management of severe acute pancreatitis. She initially presented to her local providers with severe, acute-onset abdominal pain and nausea 7 days ago. While there, workup noted a lipase level of 11,343 U/L (reference range, 10–140 U/L), and computed tomography (CT) demonstrated marked peripancreatic stranding and fluid with hypoattenuation in the head and neck suggestive of necrosis. While admitted at her local hospital, she received intravenous fluids and analgesia. While admitted at the tertiary center, she has a right upper quadrant ultrasound showing gallstones. She has been unable to tolerate an oral diet due to ongoing pain and nausea. On hospital day 6, she develops fever to 38.5°C and tachycardia to 101 bpm. She receives fluids and is started on vancomycin and ciprofloxacin. Urinalysis and chest radiograph are normal. Repeat CT shows the following.



Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	2.4	3.5-5.5
Alkaline phosphatase, serum, U/L	118	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	34	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	21	10-40
Bilirubin, total, serum, mg/dL	1.5	0.3-1.0
Blood urea nitrogen (BUN), serum or plasma, mg/dL	23	8-20
Calcium, serum, mg/dL	8.0	8.6-10.2
Carbon dioxide content, serum, mEq/L		23-30
Chloride, serum, mEq/L	118	98-106
Creatinine, serum, mg/dL	0.6 (baseline, 1.4)	0.7-1.5
Glucose, plasma (fasting), mg/dL	97	70-99
Hemoglobin, blood, g/dL	12.1	14-18
Lactic acid, serum, mmol/L		0.7-2.1
Leukocyte (WBC) count, cells/ μ L	17,000	4000-11,000
Platelet count, plt/μ L	121,000	150,000-450,000
Potassium, serum, mEq/L	4.7	3.5-5.0
Sodium, serum, mEq/L	137	136-145

She is then transferred to a tertiary care center for ongoing management. On transfer, her vitals are: temperature, 37.7°C; heart rate, 96 bpm; blood pressure, 108/54 mmHg; respiratory rate, 14 breaths per minute; and oxygen saturation, 95% on room air. She complains of 7/10 abdominal pain and nausea. Her examination reveals anasarca and a soft, diffusely tender abdomen with hypoactive bowel sounds.

Her laboratory results are shown above.

What is the next best step in management of this patient?

- A. Broad-spectrum antibiotics including carbapenem
- B. Cholecystectomy consultation
- C. CT-guided percutaneous aspiration
- D. Endoscopic necrosectomy
- E. Nasoenteric feeding

CORRECT ANSWER: E

RATIONALE

This patient has severe gallstone pancreatitis complicated by probable infected necrosis as documented by the gas in the fluid collection in her CT scan. Her current presentation is typical of infect-

ed necrosis, as patients present with fevers after their initial diagnosis of acute pancreatitis. In this case, the patient was appropriately transferred to a tertiary care center where she can receive care from a multidisciplinary team. She is currently stable and has no evidence of shock, so additional culture data, urgent debridement, and broadening of antibiotics are not needed at this time. She is now 7 days without nutrition, which increases her risk of further complications; thus, nasoenteric feeding is the priority. Lastly, although the underlying case of her acute pancreatitis is gallstones, she is too ill to undergo cholecystectomy, and the procedure would be inappropriate at this time.

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Baron TH, DiMaio CJ, Wang AY, Morgan KA. American Gastroenterological Association Clinical Practice Update: Management of Pancreatic Necrosis. *Gastroenterology*. 2020;158(1):67-75.e1. doi:10.1053/j.gastro.2019.07.064

Trikudanathan G, Wolbrink DRJ, van Santvoort HC, Mallery S, Freeman M, Besselink MG. Current Concepts in Severe Acute and Necrotizing Pancreatitis: An Evidence-Based Approach. *Gastroenterology*. 2019;156(7):1994-2007.e3. doi:10.1053/j.gastro.2019.01.269

Question 19

A 52-year-old hospitalized woman is being treated for acute severe pancreatitis and improves with empiric antibiotics and feeding tube placement. The patient is ultimately discharged on hospital day 18. She returns for follow-up 3 weeks later with ongoing nausea and dull abdominal pain. Computed tomography is performed, demonstrating a 20 cm x 12 cm heterogenous fluid collection compressing the stomach and duodenum. She undergoes an endoscopic necrosectomy with placement of a lumen-apposing metal stent. She has immediate relief and is now able to tolerate full diet without symptoms and has removed her nasoenteric feeding tube. She returns to the clinic 4 weeks later and repeat computed tomography shows resolution of her fluid collection. She reports losing about 40 pounds since her initial presentation but is beginning to regain her weight. She denies new gastrointestinal symptoms.

What is the next best step in management?

- A. Cholecystectomy consultation
- B. Endoscopic retrograde cholangiopancreatography
- C. Fecal elastase measurement
- D. Follow-up imaging at 4 weeks
- E. Metal stent removal

CORRECT ANSWER: E

RATIONALE

The patient underwent successful endoscopic necrosectomy and drainage of her fluid collection with radiographic and symptomatic improvement. Given improvement, the most appropriate step would be to remove her lumen-apposing metal stent (LAMS) immediately to avoid the risk of bleeding. The advent of LAMS has revolutionized the ability to effectively drain and debride peripancreatic fluid collections and necrosis. However, an important complication is catastrophic bleeding from the barbed edges cutting exposed vessels in the cyst cavity. Repeat imaging would not be indicated at this time, given the improvement in

symptoms, nor would ERCP for pancreatic duct leak be appropriate without evidence of persistent fluid collections. Although the patient needs her gallbladder removed to reduce the risk of recurrence, the most appropriate next step would be removal of her LAMS before surgical consultation. Lastly, it is not uncommon for a patient to lose a significant amount of weight with acute pancreatitis, and 50% of patients may develop symptoms of exocrine pancreatic insufficiency, but fecal elastase measurement is not appropriate in the absence of symptoms of steatorrhea.

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Brimhall B, Han S, Tatman PD, et al. Increased Incidence of Pseudoaneurysm Bleeding With Lumen-Apposing Metal Stents Compared to Double-Pigtail Plastic Stents in Patients With Peripancreatic Fluid Collections. *Clin Gastroenterol Hepatol*. 2018;16(9):1521-1528. doi:10.1016/j.cgh.2018.02.021

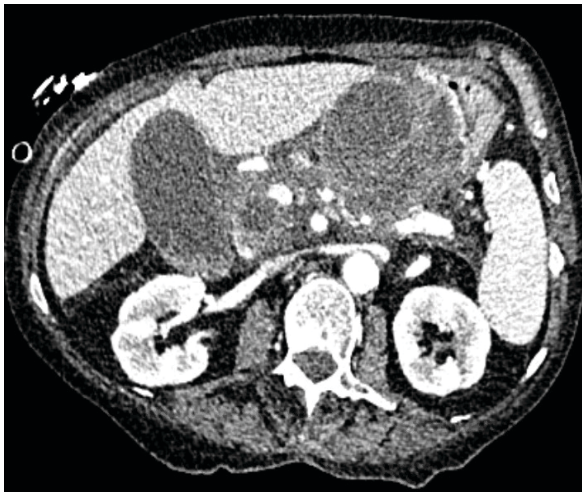
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Question 20

A 72-year-old woman with a history of alcohol-induced acute pancreatitis with resultant chronic pancreatitis presents to the emergency department with sudden-onset abdominal pain and nausea. She was recently hospitalized 3 weeks ago with acute on chronic pancreatitis complicated by a peripancreatic fluid collection. Symptoms began 10 hours before admission. She feels weak and is lightheaded. Initial vital signs include: temperature, 37.3°C; heart rate, 131 bpm; blood pressure, 80/43 mmHg; respiratory rate, 14 breaths per minute; and oxygen saturation, 98% on room air. Examination is notable for an ill-appearing female with diffuse abdominal tenderness without rebound or guarding.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	198	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	98	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	65	10-40
Bilirubin, total, serum, mg/dL	1.0	0.3-1.0
Chloride, serum, mEq/L	102	98-106
Glucose, plasma (fasting), mg/dL	74	70-99
Hemoglobin, blood, g/dL	8.7	14-18
Lactic acid, serum, mmol/L	3.6	0.7-2.1
Leukocyte (WBC) count, cells/ μ L	17,000	4000-11,000
Lipase, serum, U/L	189	10-140
Platelet count, plt/ μ L	110,000	150,000-450,000
Potassium, serum, mEq/L	3.2	3.5-5.0
Sodium, serum, mEq/L	139	136-145

Laboratory results are above. Computed tomography is performed demonstrating the results shown below.



Which of the following is the appropriate next step in management?

- Consultation with intervention radiology
- Endoscopic drainage of fluid collection
- Endoscopic retrograde cholangiopancreatography for a pancreatic duct leak
- Intensive care admission for resuscitation and close monitoring
- Magnetic resonance imaging with cholangiopancreatography

CORRECT ANSWER: A

RATIONALE

This patient is presenting with acute-onset abdominal pain in the context of a recent history of acute pancreatitis with fluid collections. Computed tomography shows a cyst filled with heterogeneous material concerning for acute blood products. Given her anemia and hypotension, bleeding from a pseudoaneurysm should be considered and as such consultation with interventional radiology is most appropriate. Endoscopic drainage would be contraindicated. Although it is possible that the initial fluid collection may be from an underlying pancreatic duct leak, pursuing endoscopic retrograde cholangiopancreatography at this moment would not be appropriate given the concern for bleeding. Although the patient is ill and will need close monitoring, intensive care admission without intervention would be incorrect. Lastly, although further imaging may be needed, it should be directed by interventional radiology to determine how best to address a suspected pseudoaneurysm. Thus, magnetic resonance imaging with cholangiopancreatography would not be appropriate without further discussion.

REFERENCE

Chiang KC, Chen TH, Hsu JT. Management of chronic pancreatitis complicated with a bleeding pseudoaneurysm. *World J Gastroenterol*. 2014;20(43):16132-16137. doi:10.3748/wjg.v20.i43.16132

Question 21

A 46-year-old woman presents to a gastroenterologist for evaluation and management of pancreatitis after a recent hospitalization 2 weeks ago. The patient has a longstanding history of tobacco and alcohol abuse. She was recent admitted to a local hospital for abdominal pain and nausea and, during this hospitalization, was given a diagnosis of acute pancreatitis. She was managed conservatively with fluids and discharged on hospital day 4. In review of the records, computed tomography performed at admission showed peripancreatic inflammation around the head and uncinate process of the pancreas with scattered coarse calcifications and an irregular pancreatic duct. Magnetic resonance imaging, also performed during this hospitalization, confirmed a diagnosis of chronic pancreatitis and showed evidence of an isolated splenic vein thrombosis. Currently the patient feels well and has no complaints. She continues to smoke and drink. She denies a history of blood clots or a family history of thrombophilia. Her most recent complete blood count, evaluated last week, was normal.

What is the next best step in management?

- A. Anticoagulation therapy
- B. Hematology referral
- C. Short-interval repeat imaging
- D. Surgical referral
- E. Upper endoscopy

CORRECT ANSWER: C

RATIONALE

According to a 10-year retrospective review, the incidence of splanchnic vein thrombosis in patients with acute pancreatitis is as low as 2%, with the majority of thromboses involving the splenic vein. In this review, there was no significant difference in recanalization rates for patients on anticoagulation. For these reasons, short-interval repeat imaging is preferred over initiation of anticoagulation. In the absence of a personal or family history of thrombophilia, the cause of splenic vein throm-

bosis is from her underlying pancreatitis; thus, hematology referral is not needed at this time. Lastly, with splenic vein thromboses, isolated gastric varices can occur; however, in the absence of bleeding and without plans for anticoagulation, upper endoscopy is not needed.

REFERENCE

Ejikeme C, Elkattawy S, Kayode-Ajala F, Al-Nasreri A, Naik A. Acute Pancreatitis Induced Splenic Vein Thrombosis. *Cureus*. 2021;13(6):e15714. Published 2021 Jun 17. doi:10.7759/cureus.15714

Harris S, Nadkarni NA, Naina HV, Vege SS. Splanchnic vein thrombosis in acute pancreatitis: a single-center experience. *Pancreas*. 2013;42(8):1251-1254. doi:10.1097/MPA.0b013e3182968ff5

Question 22

A 56-year-old man presents for evaluation to a gastroenterologist for nausea and abdominal pain. The patient was admitted to a local hospital 4 weeks ago with acute pancreatitis. He reports that he received fluids and pain medications and was discharged on hospital day 5 after being started on an oral diet. Since discharge, he has dull postprandial upper abdominal pain and nausea but notes that his weight has been stable. Computed tomography is performed showing hypoattenuation of the neck and body of the pancreas with normal enhancement and stranding around the tail of the pancreas. There is a 2.3 cm x 1.1 cm fluid collection abutting the stomach in the region of the body of the pancreas.

What is the next step in management?

- A. Endoscopic fluid drainage
- B. Endoscopic retrograde cholangiopancreatography with pancreatic duct stenting
- C. Magnetic resonance imaging with cholangiopancreatography
- D. Nasoenteric feeding
- E. Surgical consultation

CORRECT ANSWER: E

RATIONALE

This patient is presenting after a recent episode of acute pancreatitis with follow-up imaging suggestive of disconnected duct syndrome with a remnant tail resulting in ongoing inflammation and fluid drainage due to the sequestered tail. The most appropriate management here would be surgical consultation for resection. The fluid collection is too small for drainage, and endoscopic drainage is unlikely to resolve the underlying issue. Endoscopic retrograde cholangiopancreatography can be considered, especially in patients who are not surgical candidates; however, with complete disruption, stenting is unlikely to be feasible and thus should not be considered before surgical consultation. Although further imaging may better characterize the disruption, the computed tomography results and clinic picture are consistent with disconnected duct syndrome. Thus, further imaging with magnetic resonance imaging would be excessive. Lastly, although the patient is having postprandial symptoms, his weight is stable, so nasoenteric feeding is not needed at this time.

REFERENCE

Baron TH, DiMaio CJ, Wang AY, Morgan KA. American Gastroenterological Association Clinical Practice Update: Management of Pancreatic Necrosis. *Gastroenterology*. 2020;158(1):67-75.e1. doi:10.1053/j.gastro.2019.07.064

Trikudanathan G, Wolbrink DRJ, van Santvoort HC, Mallory S, Freeman M, Besselink MG. Current Concepts in Severe Acute and Necrotizing Pancreatitis: An Evidence-Based Approach. *Gastroenterology*. 2019;156(7):1994-2007.e3. doi:10.1053/j.gastro.2019.01.269

Question 23

A 35-year-old man presents for recurrent acute pancreatitis. The patient reports at least 25 hospitalizations for recurrent acute pancreatitis over the last 10 years. Each time he presents

with acute-onset pain and is noted to have lipase values that are greater than 10 times the normal limit. His workup has included multiple cross-sectional images and endoscopic ultrasounds. He denies alcohol or tobacco use and is not on any medications.

He was adopted and does not know his birth parents. He and his wife have been unsuccessful in having children.

What is the next best step in management?

- A. Genetic testing
- B. Empiric cholecystectomy
- C. Empiric steroid trial
- D. Endoscopic retrograde cholangiopancreatography with manometry
- E. Total pancreatectomy with islet autotransplantation

CORRECT ANSWER: A

RATIONALE

This patient is presenting with recurrent acute pancreatitis and infertility, suggestive of an underlying *CFTR* (cystic fibrosis transmembrane conductance regular) mutation that likely increases his risk of acute pancreatitis and leads to bilateral absence of the vas deferens. Thus, genetic testing should be pursued before endoscopic retrograde cholangiopancreatography or total pancreatectomy. There is no role for empiric steroids especially in the absence of other features suggestive of autoimmune pancreatitis. Lastly, some data suggest that empiric cholecystectomy can reduce recurrent episodes of acute pancreatitis, but this should only be considered after genetic testing has been completed.

REFERENCE

Abu-El-Haija M, Valencia CA, Hornung L, et al. Genetic variants in acute, acute recurrent and chronic pancreatitis affect the progression of disease in children. *Pancreatology*. 2019;19(4):535-540. doi:10.1016/j.pan.2019.05.001

Question 24

A 23-year-old man with cystic fibrosis has multiple hospitalizations for recurrent acute pancreatitis. He presents in clinic for dull abdominal pain that occurs between these episodes. During his last hospitalization, he was told for the first time that his blood sugars were in the “prediabetic” range. He is concerned about the long-term consequences of his recurrent episodes of acute pancreatitis and inquires about measures to prevent episodes.

What would be the most appropriate next step in management?

- A. Continuous glucose monitoring
- B. Long-acting opioids for pain management
- C. Pancreatic enzyme replacement therapy
- D. Referral for total pancreatectomy with islet autotransplantation
- E. Steroid trial for autoimmune pancreatitis

CORRECT ANSWER: D**RATIONALE**

This patient continues to have recurrent episodes of acute pancreatitis and is now showing signs of chronic pancreatitis and perhaps even type 3c diabetes. In these cases, it is best for patients to be referred to a specialty center for consideration of total pancreatectomy with islet autotransplantation to reduce the need for long-term opioids and to increase the yield of functioning islets. Indeed, this patient is having pain; however, nonnarcotic pain medications should be used first. There is no evidence of pancreatic insufficiency; thus, pancreatic enzyme replacement is not indicated. Steroids are not indicated in the absence of features of autoimmune pancreatitis. Lastly, continuous

glucose monitoring may be needed but would be best directed by endocrinology, and this is the first instance of abnormal blood sugars.

REFERENCE

Bellin MD, Kerdsirichairat T, Beilman GJ, et al. Total Pancreatectomy With Islet Autotransplantation Improves Quality of Life in Patients With Refractory Recurrent Acute Pancreatitis. *Clin Gastroenterol Hepatol*. 2016;14(9):1317-1323. doi:10.1016/j.cgh.2016.02.027

Question 25

A 69-year-old man with a history of tobacco use presents to his primary care physician with painless jaundice and a 9 kg weight loss. He does not take medication. He has smoked 2 packs of cigarettes daily for the last 50 years. He drinks moderately, having 4 to 6 beers daily, but denies illicit drug use. He has no family history of pancreatic disease. His examination is notable for jaundice and mild tenderness in the right upper quadrant and epigastric area. Laboratory results are notable for a normal complete blood count and basic metabolic panel. His liver test results are below.

Computed tomography shows intra- and extrahepatic biliary duct dilatation with transition at the level of the pancreatic head without a clear mass identified. The patient is referred to gastroenterology. Endoscopic ultrasound reveals a mass-like lesion, which is biopsied and shows marked chronic inflammation and fibrosis compatible with chronic pancreatitis. Endoscopic retrograde cholangiopancreatography demonstrates a severe stricture in the distal common bile duct, which was brushed, and a plastic stent was placed. Brushings are

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	415	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	154	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	184	10-40
Bilirubin, serum, mg/dL	10.1	0.3-1.0
Total	8.4	0.1-0.3
Direct		

negative. The serum carbohydrate antigen 19-9 level is elevated at 100 U/mL (reference range, 0-37 U/mL), and the immunoglobulin G4 level is also elevated at 250 mg/dL (reference range, 2.4-121.0 mg/dL).

What is the next best step in management?

- A. Computed tomography in 3 months
- B. Endoscopic ultrasound with fine-needle biopsy
- C. Oncology consultation for neoadjuvant therapy
- D. Steroid therapy for autoimmune pancreatitis
- E. Surgical consultation for resection

CORRECT ANSWER: B

RATIONALE

This patient is presenting with obstructive jaundice and weight loss and likely has malignancy unless proven otherwise. Thus, the correct answer would be repeat endoscopic ultrasound and biopsy. Although some providers may consider repeat short-interval imaging with computed tomography in 3 months, repeat biopsy should be considered first. Without definitive diagnosis, it would be incorrect to pursue steroid treatment for autoimmune pancreatitis based on an elevated serum immunoglobulin G4 level or neoadjuvant chemotherapy because of an elevated carbohydrate antigen 19-9 level. Lastly, if repeat biopsy is negative, surgical referral for possible resection can be considered; however, given the high concern for malignancy, repeat biopsy should be considered first.

REFERENCE

Majumder S, Takahashi N, Chari ST. Autoimmune Pancreatitis. *Dig Dis Sci*. 2017;62(7): 1762-1769. doi:10.1007/s10620-017-4541-y

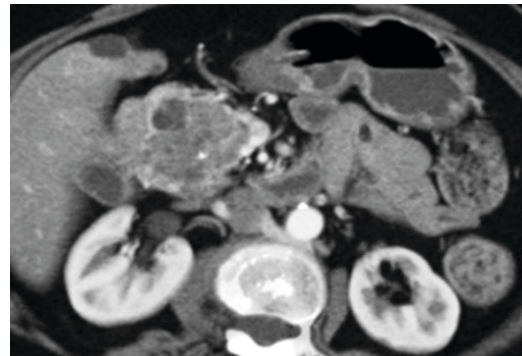
Question 26

A 62-year-old woman presented to clinic for evaluation of an incidental finding of a pancreatic head

mass. She underwent computed tomography (CT) of the abdomen for evaluation of hematuria, given concern for a kidney stone. CT revealed a mass in the head of the pancreas. A pancreatic protocol CT was subsequently performed for further evaluation and showed a well-demarcated multicystic lesion in the head of the pancreas with central calcification (Figure A). The gall bladder and biliary tree were noted to be normal. Laboratory tests revealed a normal liver panel and serum carbohydrate antigen 19-9 level. She is currently asymptomatic, and abdominal examination is unremarkable. She denies history of pancreatitis or a family history of pancreatic cancer. An endoscopic ultrasound is performed with fine-needle aspiration of one of the larger cysts, and fluid analysis shows carcinoembryonic antigen level of less than 5 ng/mL.

What is the next best step in management?

Figure A



- A. Endoscopic retrograde cholangiopancreatography with stent placement
- B. Follow-up with CT or magnetic resonance imaging in 3-6 months
- C. Reassurance and no intervention
- D. Refer to surgery for pancreaticoduodenectomy
- E. Send out cyst fluid for DNA-based molecular testing

CORRECT ANSWER: C

RATIONALE

This patient has a typical microcystic serous cystadenoma with characteristic imaging find-

ings on CT scan with a honey-comb appearance and central calcifications. The endosonographic appearance is characteristic of a serous cystadenoma, and fine-needle aspiration is not required for diagnosis. Patients should be reassured; in the absence of symptoms, these cysts do not need surgical resection or close surveillance.

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Elta GH, Enestvedt BK, Sauer BG, Lennon AM. ACG Clinical Guideline: Diagnosis and Management of Pancreatic Cysts. *Am J Gastroenterol*. 2018;113(4):464-479. doi:10.1038/ajg.2018.14

Megibow AJ. Update in imaging of cystic pancreatic masses for gastroenterologists. *Clin Gastroenterol Hepatol*. 2008;6(11):1194-1197. doi:10.1016/j.cgh.2008.08.026

Question 27

A 60-year-old man with long-standing tobacco use, mild chronic obstructive pulmonary disease, and hypertension underwent low-dose computed tomography (CT) of the chest for lung cancer screening. The CT showed a 2-cm cyst in the body of the pancreas and a 1-cm cyst in the head of the pancreas. The patient is asymptomatic and denies history of pancreatitis or family history of pancreatic cancer.

What is the next best step in his evaluation?

- A. Contrast-enhanced magnetic resonance imaging (MRI) with cholangiopancreatography
- B. Endoscopic ultrasound with possible fine-needle aspiration
- C. MRI or pancreatic protocol CT in 1 year
- D. MRI or pancreatic protocol CT in 6 mos
- E. Referral to surgery

CORRECT ANSWER: A

RATIONALE

A dedicated MRI with cholangiopancreatography is the recommended modality of choice for initial

evaluation of incidentally found pancreatic cysts and allows for diagnosis of cyst type based on cyst characteristics, communication with main duct, and other factors, as well as for identification of high-risk features such as pancreatic ductal dilation and mural nodules. Although endoscopic ultrasound or pancreatic protocol CT is an excellent alternative to MRI, the low-dose CT scan performed in this instance may not characterize the cyst well enough to evaluate for high-risk features.

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Question 28

A 65-year-old woman is seen for follow-up after a recent hospitalization for mild acute pancreatitis. Magnetic resonance cholangiopancreatography was performed during her hospitalization to evaluate for choledocholithiasis, which did not reveal any stones within the bile duct. However, the main pancreatic duct was noted to be dilated to 13 mm. Endoscopy revealed the following appearance of the ampulla (Figure A) and endoscopic ultrasound revealed dilated main pancreatic duct without any mass lesions within the pancreas (Figure B). What is the next best step in management?

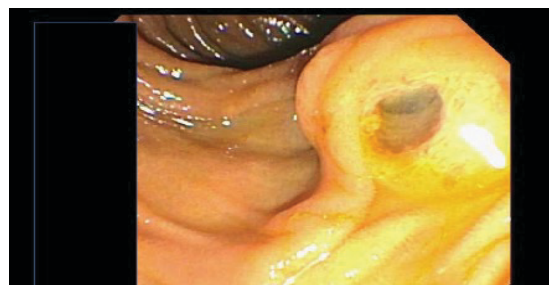


Figure A



Figure B

- A. Endoscopic retrograde cholangiopancreatography with pancreatoscopy
- B. Fine-needle aspiration by endoscopic ultrasound
- C. Magnetic resonance imaging with cholangiopancreatography in 3 months
- D. Pancreatic protocol computed tomography in 3 months
- E. Referral to surgery

CORRECT ANSWER: E

RATIONALE

The patient likely has main duct intraductal papillary mucinous neoplasm (MD-IPMN). The frequency of high-grade dysplasia and invasive carcinoma in MD-IPMN is over 60%. Surgical resection is strongly recommended for all surgically fit patients with a main pancreatic duct greater than 10 mm and is preferable to short-term surveillance. ERCP with or without pancreatoscopy or fine-needle aspiration via endoscopic ultrasound are not routinely indicated in evaluation of patients with MD-IPMN. Delayed imaging in 3 months with magnetic resonance imaging or computed tomography would not be recommended with the possibility of high-grade dysplasia.

REFERENCE

Tanaka M, Fernández-Del Castillo C, Kamisawa T, et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. *Pancreatology*. 2017;17(5):738-753. doi:10.1016/j.pan.2017.07.007

Question 29

A 75-year-old man with obesity, hypertension, type 2 diabetes mellitus, chronic obstructive pulmonary disease, history of cerebrovascular accident with right hemiparesis, and non-ST elevation myocardial infarction 6 months ago is referred to you for evaluation of an incidentally found cystic lesion in the uncinate process of the pancreas (Figure A). His calculated Charlson comorbidity index score is 9. The lesion was evaluated with magnetic resonance imaging, which revealed a 3.5-cm cystic lesion communicating with the pancreatic duct (Figure B). Laboratory evaluation shows normal liver panel and normal carbohydrate antigen 19-9 level. What is the best recommendation for management of his pancreatic cyst?

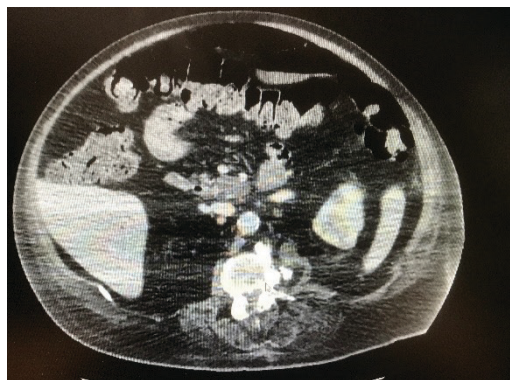


Figure A

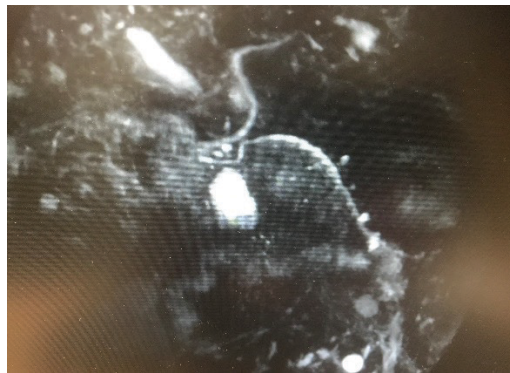


Figure B

- A. Endoscopic ultrasound with fine-needle aspiration of the cyst
- B. Magnetic resonance imaging follow-up
- C. No further evaluation
- D. Surgical resection

CORRECT ANSWER: C**RATIONALE**

Clinical scoring systems such as the Charlson comorbidity index score can predict 10-year survival rates for patients with multiple comorbidities and can identify patients with a high likelihood of non-IPMN-related death within 3 years of diagnosis. The patient in this clinical scenario has multiple comorbidities and is unlikely to be a surgical candidate. The 2018 American College of Gastroenterology guidelines recommend that patients who are not medically fit for surgery should not undergo further evaluation of incidentally found pancreatic cysts, irrespective of cyst size; thus, endoscopic ultrasound nor magnetic resonance imaging would be indicated.

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Elta GH, Enestvedt BK, Sauer BG, Lennon AM. ACG Clinical Guideline: Diagnosis and Management of Pancreatic Cysts. *Am J Gastroenterol*. 2018;113(4):464-479. doi:10.1038/ajg.2018.14

Sahora K, Ferrone CR, Brugge WR, et al. Effects of Comorbidities on Outcomes of Patients With Intraductal Papillary Mucinous Neoplasms. *Clin Gastroenterol Hepatol*. 2015;13(10):1816-1823. doi:10.1016/j.cgh.2015.04.177

Question 30

A 65-year-old man with obesity, hypertension, and diabetes mellitus presents for follow-up of a pancreatic cyst. He was seen about a year ago, and contrast-enhanced magnetic resonance imaging (MRI) with cholangiopancreatography showed a 1.5-cm cyst in the uncinate process of the pancreas with possible communication to the pancreatic duct. He denied history of pancreatitis or family history of pancreatitis. A 1-year follow-up with MRI was recommended.

The most recent MRI shows a cyst size of 2.5 cm without any mural nodules, cyst wall enhancement, or pancreatic duct dilation. The patient

remains asymptomatic and denies weight loss. Which of the following is the next best step in management?

- A. Obtain carbohydrate antigen 19-9 level
- B. Perform endoscopic ultrasound with/without fine-needle aspiration
- C. Refer to surgery for pancreaticoduodenectomy
- D. Repeat MRI in 6-12 months

CORRECT ANSWER: B**RATIONALE**

Worrisome features on imaging include cyst size greater than 3 cm, enhancing mural nodules less than 5 mm, thickened or enhancing cyst wall, cyst size growth of greater than 5 to 6 mm within 2 years, main pancreatic duct (MPD) size of 5 to 9 mm, abrupt change in the MPD caliber. These patients should be evaluated by endoscopic ultrasonography to further stratify the lesion. The role of serum carbohydrate antigen 19-9 testing is not well defined in management of pancreatic cystic lesions. Although this could be considered, the best next step in evaluating this patient would be an endoscopic ultrasound examination with possible fine-needle biopsy. Cysts without these features can continue to be followed up with cross-sectional imaging, whereas cysts with high-risk features such as obstructive jaundice, enhancing mural nodules 5 mm or greater in size, and MPD size of greater than 10 mm should undergo resection.

REFERENCES

Elta GH, Enestvedt BK, Sauer BG, Lennon AM. ACG Clinical Guideline: Diagnosis and Management of Pancreatic Cysts. *Am J Gastroenterol*. 2018;113(4):464-479. doi:10.1038/ajg.2018.14

Tanaka M, Fernández-Del Castillo C, Kamisawa T, et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. *Pancreatol*. 2017;17(5):738-753. doi:10.1016/j.pan.2017.07.007

Question 31

A 50-year-old woman with a history of hypertension, osteoarthritis, and colonic diverticulitis presented to the emergency department with left lower quadrant abdominal pain. Computed tomography was performed and revealed sigmoid diverticulitis. Incidentally a 3.5-cm cyst was seen in the tail of the pancreas. She is referred to gastroenterology for further evaluation and management. An endoscopic ultrasound and fine-needle aspiration are subsequently performed. Cyst fluid analysis reveals the following: carcinoembryonic antigen (CEA), 1400 ng/mL; amylase, 50 IU/mL; glucose, 5 mg/dL; cytology, scant cellularity; molecular markers, *KRAS* mutation.

Which one of the following is the most likely diagnosis?

- A. Mucinous cystic neoplasm
- B. Pseudocyst
- C. Serous cystadenoma
- D. Cystic neuroendocrine tumor

CORRECT ANSWER: A

RATIONALE

Cyst fluid CEA is useful in differentiating mucinous from nonmucinous cysts. A cyst fluid CEA cut-off of greater than 192 ng/mL is commonly used, and very high levels greater than 800 ng/mL are highly specific for intraductal papillary mucinous neoplasm and mucinous cystic neoplasms. Pseudocysts have high amylase levels along with very low CEA levels. Cyst fluid CEA levels are low (<5 ng/mL) in serous cystadenomas. Cyst fluid CEA is not helpful for identifying the presence of high-grade dysplasia or pancreatic cancer. *KRAS* mutations favor mucinous differentiation.

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Khalid A, Zahid M, Finkelstein SD, et al. Pancreatic cyst fluid DNA analysis in evaluating pancreatic cysts: a report of the PANDA study. *Gastrointest Endosc*. 2009;69(6):1095-1102. doi:10.1016/j.gie.2008.07.033

Question 32

A 65-year-old man is found to have an incidental pancreatic cystic lesion measuring 1.5 cm in the body of the pancreas. Magnetic resonance imaging is performed and confirms a 1.5-cm cyst with communication to the main pancreatic duct. No mural nodules or wall thickening is noted. In addition, several small cysts are scattered throughout the head and body of the pancreas. The main pancreatic duct is nondilated. The patient is asymptomatic and is overall healthy except for mild hypertension and obesity. He denies history of pancreatitis or a family history of pancreatic cancer.

What is the best recommendation for further evaluation and follow-up of this cyst?

- A. Endoscopic ultrasound (EUS) in 1 year
- B. EUS with fine-needle aspiration
- C. Magnetic resonance imaging (MRI) in 1 year
- D. Reassurance and no surveillance
- E. Surgical referral

CORRECT ANSWER: C

RATIONALE

This patient most likely has multiple branch duct intraductal papillary mucinous neoplasms. Guidelines recommend surveillance for cysts less than 3 cm without high-risk features. Surveillance can be performed with cross-sectional imaging, with interval based on cyst size. MRI is preferred over EUS. Since no high-risk clinical or imaging findings are present in this case, immediate surgi-

cal referral and diagnostic EUS with fine-needle aspiration are not required.

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Elta GH, Enestvedt BK, Sauer BG, Lennon AM. ACG Clinical Guideline: Diagnosis and Management of Pancreatic Cysts. *Am J Gastroenterol*. 2018;113(4):464-479. doi:10.1038/ajg.2018.14

Vege SS, Ziring B, Jain R, Moayyedi P; Clinical Guidelines Committee; American Gastroenterology Association. American gastroenterological association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. *Gastroenterology*. 2015;148(4):819-22. doi:10.1053/j.gastro.2015.01.015

Question 33

A 60-year-old woman is noted to have a 1.5-cm ovoid hypodense lesion within the pancreatic tail identified on computed tomography of the chest, performed for evaluation of chronic cough. Magnetic resonance imaging is recommended for better characterization of this lesion and reveals a 1.5-cm T2 hyperintense peripherally enhancing lesion within the pancreatic tail with persistent peripheral enhancement on delayed-phase images (Figure A). Subsequently, an endoscopic ultrasound is performed and demonstrates a 1.6-cm predominantly solid lesion at the tail of the pancreas with a central cystic component (Figure B). Fine-needle aspiration is performed.

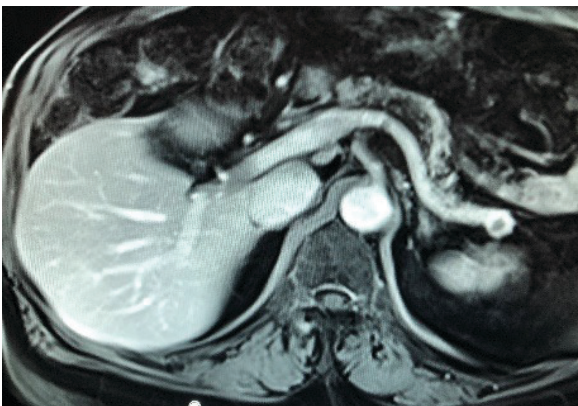


Figure A

The cyst fluid carcinoembryonic antigen level is 10 ng/mL. Cytology reveals groups of cells with eccentric nuclei with “salt and pepper” chromatin (Figure C). Immunostains are positive for CKAE1/AE3, CD56, synaptophysin, and chromogranin.

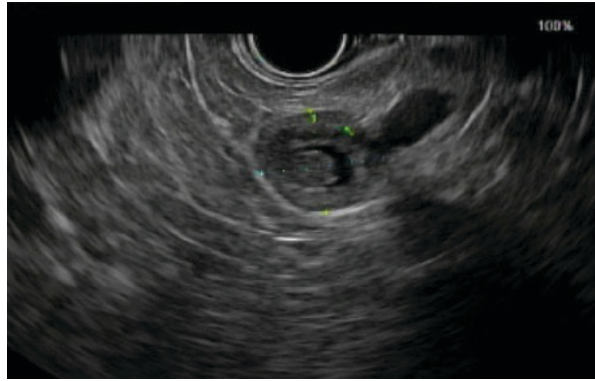


Figure B

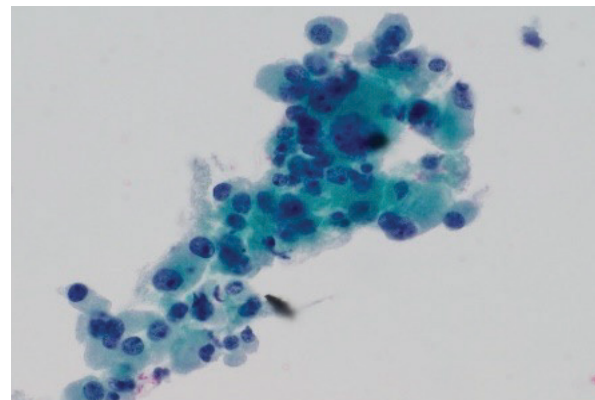


Figure C

What is the most likely diagnosis?

- A. Cystic neuroendocrine tumor
- B. Mucinous cystic neoplasm
- C. Pancreatic adenocarcinoma
- D. Serous cystadenoma
- E. Solid pseudopapillary neoplasm

CORRECT ANSWER: A

RATIONALE

Pancreatic neuroendocrine tumors can be solid, cystic, or mixed in morphology. Fine-needle aspirate is usually highly cellular and has a high diagnostic accuracy of up to 92.5%. Cytologic

evaluation often reveals sheets of uniform-appearing cells with eccentric nuclei and salt and pepper chromatin, expressing neuroendocrine markers such as synaptophysin, chromogranin A, and CD56.

REFERENCE

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Question 34

A 40-year-old man with no significant past medical history is admitted to the hospital with progressively worsening episodes of weakness, confusion, sweating, and palpitations. In the emergency department, he is found to have a blood glucose level of 30 mg/dL and is treated with a glucose load, which resolves his symptoms.

During his hospital stay, a 72-hour fast is initiated; within 12 hours, he is noted to have the following laboratory results below.

Computed tomography (CT) of the abdomen is unrevealing.

What is the next best step in his management?

- A. 68-Ga DOTATATE positron emission tomography/computed tomography (PET/CT)
- B. Arterial stimulation with venous sampling
- C. Contrast-enhanced CT
- D. Endoscopic ultrasound
- E. Octreotide scan

CORRECT ANSWER: D

RATIONALE

This patient has an insulinoma based on initial presentation with Whipple's triad (triad of symptoms, a low plasma glucose concentration, and relief by raising plasma glucose). The 72-hour fasting test with combination of an elevated proinsulin level with a fasting glucose less than 45 mg/dL is diagnostic of an insulinoma. When cross-sectional imaging modalities such as CT or magnetic resonance imaging fail to localize the tumor, endoscopic ultrasound is the diagnostic modality of choice, and use of fine-needle aspiration can also help to establish a histopathologic diagnosis. Further CT modalities would not be helpful. The 68-Ga DOTATATE PET/CT is a somatostatin receptor-based imaging technique usually reserved for small bowel neuroendocrine tumors, such as carcinoid.

REFERENCE

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Question 35

A 52-year-old man presents with recurring peptic ulcer disease and diarrhea.

Which of these hereditary syndromes is most commonly associated with this patient's diagnosis?

- A. Multiple endocrine neoplasia 1 (MEN1)
- B. Multiple endocrine neoplasia 2A (MEN2A)
- C. Multiple endocrine neoplasia 2B (MEN2B)
- D. Neurofibromatosis (NF1)
- E. von Hippel-Lindau (VHL) syndrome

Laboratory Test	Result	Reference Range
C peptide, serum, ng/mL	7	0.8-3.1
Glucose, plasma (fasting), mg/dL	35	70-99
Insulin, serum (fasting), μ U/mL	27	<20
Proinsulin, serum, pmol/L	1000	3-20

CORRECT ANSWER: A**RATIONALE**

Hereditary endocrinopathies such as MEN1, VHL syndrome, and (NF1) can be associated with pNETs. The most important is MEN1 because 80% to 100% of these patients develop nonfunctioning pNETs, 50% to 60% develop gastrinomas, and 20% develop insulinomas. MEN2A and MEN2B are not associated with pNETs, but rather medullary thyroid cancer, pheochromocytoma, primary parathyroid hyperplasia (MEN2A) or medullary thyroid cancer and pheochromocytoma (MEN2B).

REFERENCE

Metz DC, Jensen RT. Gastrointestinal neuroendocrine tumors: pancreatic endocrine tumors. *Gastroenterology*. 2008;135(5):1469-1492. doi:10.1053/j.gastro.2008.05.047

Question 36

A 56-year-old woman is admitted to the hospital for a second episode of pancreatitis in the past 3 months. She denies a history of alcohol use. During these episodes, her liver function panel is normal, and right upper quadrant ultrasound reveals no cholelithiasis or choledocholithiasis. Serum triglyceride and calcium levels are within normal limits. Her past medical history is significant for hypertension, uterine fibroids, and obesity. Computed tomography performed during the initial episode of pancreatitis revealed a 2-cm cyst in the uncinate process of the pancreas. Magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography is performed and reveals a 2-cm cyst in the uncinate communicating with a normal-caliber pancreatic duct. No solid component is visualized inside the cyst.

What is the next best step in this patient's management?

- A. Endoscopic retrograde cholangiopancreatography

- B. Endoscopic ultrasound with fine-needle aspiration
- C. Genetic testing
- D. Repeat MRI in 6 months
- E. Surgical referral

CORRECT ANSWER: E**RATIONALE**

Based on results of MRI, this patient likely has a branch duct intraductal papillary mucinous neoplasm, which is contributing to recurrent pancreatitis. A repeat MRI in 6 months would not be useful, and endoscopic retrograde cholangiopancreatography and endoscopic ultrasound with fine-needle aspiration would likely not add significantly more information than current MRI/magnetic resonance cholangiopancreatography. Recurrent pancreatitis is considered to be a high-risk feature, with acute pancreatitis, secondary to the cyst being associated with increased risk of cancer. These patients should be referred to a multidisciplinary group with consideration of surgical resection. In addition, surgery may be needed for relief of symptoms as well.

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Elta GH, Enestvedt BK, Sauer BG, Lennon AM. ACG Clinical Guideline: Diagnosis and Management of Pancreatic Cysts. *Am J Gastroenterol*. 2018;113(4):464-479. doi:10.1038/ajg.2018.14

Tanaka M, Fernández-Del Castillo C, Kamisawa T, et al. Revisions of international consensus Fukuoka guidelines for the management of IPMN of the pancreas. *Pancreatology*. 2017;17(5):738-753. doi:10.1016/j.pan.2017.07.007

Question 37

A 50-year-old man presents for evaluation of ongoing upper abdominal pain for 2 years. He reports chronic postprandial epigastric pain with intermittent radiation to the back. He has had 1 hospital admission for abdominal pain 6 months ago and was diagnosed with mild acute

pancreatitis. Over the past few months, he reports change in bowel habits with constipation alternating with diarrhea. He denies unintentional weight loss. He reports heavy alcohol intake in the past with recent decrease but continues to drink approximately 25 oz of alcohol daily. He smokes half a pack of cigarettes daily. His past medical history is significant for obesity, type 2 diabetes mellitus, and hypertension. He denies family history of gastrointestinal malignancy. Examination reveals mild epigastric tenderness to palpation. Computed tomography is ordered for evaluation of chronic pancreatitis and is unrevealing.

What is the next best test for diagnosis of chronic pancreatitis?

- A. Endoscopic ultrasound
- B. Fecal elastase level
- C. Genetic testing
- D. Quantitative 72-hour fecal fat collection
- E. Secretin-enhanced magnetic resonance cholangiopancreatography

CORRECT ANSWER: A

RATIONALE

Cross-sectional imaging with computed tomography or magnetic resonance imaging are first-line investigations for diagnosing chronic pancreatitis. If these imaging modalities are not diagnostic, endoscopic ultrasound should be used as the next line of investigation. The 2020 American College of Gastroenterology guidelines for chronic pancreatitis recommend secretin-enhanced magnetic resonance cholangiopancreatography for the diagnosis of chronic pancreatitis only if cross-sectional imaging or endoscopic ultrasound do not confirm the diagnosis and the clinical suspicion remains high. Fecal elastase evaluation and quantitative fecal fat collection can help with diagnosing exocrine pancreatic insufficiency. However, the sensitivity of pancreatic function testing to make the diagnosis of chronic pancreatitis is low and should be used only as an ancillary test in making the diagnosis. With no family history and alcohol use

disorder present, genetic testing would be lower on the differential.

REFERENCE

Gardner TB, Adler DG, Forsmark CE, Sauer BG, Taylor JR, Whitcomb DC. ACG Clinical Guideline: Chronic Pancreatitis. *Am J Gastroenterol*. 2020;115(3):322-339. doi:10.14309/ajg.0000000000000535

Question 38

A 45-year-old man with chronic pancreatitis related to alcohol use presents with altered bowel habits for the past few months. He reports 3 to 4 bowel movements daily, which are loose, non-bloody, and foul smelling. He notes an “oil slick” in the toilet bowl and difficulty flushing the stool. He reports a 5-pound weight loss during this time. His physical examination is remarkable for mild tenderness to palpation in the epigastric and right upper quadrants. Laboratory tests reveal normal complete blood count and serum amylase and lipase levels. Stool studies reveal no infectious etiology for chronic diarrhea. A 72-hour fecal fat collection shows steatorrhea. The fecal elastase level is less than 15 µg/mL.

What is the best treatment option for this patient’s condition?

- A. Low-fat diet with <50 g fat daily
- B. Low-fat diet with <30 g fat daily
- C. Pancreatic enzyme replacement with 20,000-30,000 USP units of lipase with each meal
- D. Pancreatic enzyme replacement with 40,000-50,000 USP units of lipase with each meal

CORRECT ANSWER: D

RATIONALE

The most effective treatment option for exocrine pancreatic insufficiency is pancreatic enzyme replacement therapy. A starting dose of 40,000 to

50,000 USP units of lipase is recommended with dose increase up to 90,000 USP units of lipase based on response to treatment. Although small frequent meals and a low-fat diet can help with symptoms, extreme fat restriction can be detrimental and lead to fat-soluble vitamin deficiencies. Pancreatic enzyme replacement therapy is essential for optimizing nutritional status of patients with exocrine pancreatic insufficiency.

REFERENCE

Gardner TB, Adler DG, Forsmark CE, Sauer BG, Taylor JR, Whitcomb DC. ACG Clinical Guideline: Chronic Pancreatitis. *Am J Gastroenterol.* 2020;115(3):322-339. doi:10.14309/ajg.0000000000000535

Question 39

A 60-year-old woman with idiopathic chronic pancreatitis presents with progressively worsening abdominal pain over the past year. She has used nonsteroidal antiinflammatory drugs as needed in the past. Her primary care physician prescribed tramadol and, most recently, gabapentin for her pain. She continues to have chronic abdominal pain ranging from 5/10 to 7/10 in intensity and finds the pain to be interfering with her work and quality of life. Magnetic resonance imaging with magnetic resonance cholangiopancreatography is performed and shows irregular contour of the pancreatic duct but no ductal dilation or calcifications.

What is the next best option for management of her pain?

- A. Endoscopic retrograde cholangiopancreatography with stent placement
- B. Endoscopic-guided celiac plexus block
- C. Long-term opiate therapy
- D. Pancreatic enzyme replacement therapy
- E. Total pancreatectomy with islet autotransplantation

CORRECT ANSWER: B

RATIONALE

This patient has chronic pancreatitis with pain that has been uncontrolled with opiate-sparing analgesics and gabapentinoid adjuncts. In these patients with chronic pancreatitis-related pain, who have failed initial medical management, celiac plexus block via endoscopic ultrasound should be considered. Although the median response rate of this procedure is around 68% and it needs to be repeated every few months, it is relatively low risk and represents an opiate-free pathway for pain relief in patients with chronic pancreatitis. Since there are no ductal obstructions or dilation, endoscopic retrograde cholangiopancreatography with stent placement will not be helpful. Opiate therapy may be considered to treat painful chronic pancreatitis but only in patients for whom all other reasonable therapeutic options have been exhausted. Pancreatic enzyme replacement therapy does not lead to significant improvement in pain from chronic pancreatitis. Total pancreatectomy with islet autotransplantation is not widely available and can be considered in younger patients with intractable pain who have failed all other management options.

REFERENCES

Gardner TB, Adler DG, Forsmark CE, Sauer BG, Taylor JR, Whitcomb DC. ACG Clinical Guideline: Chronic Pancreatitis. *Am J Gastroenterol.* 2020;115(3):322-339. doi:10.14309/ajg.0000000000000535

Park, WY, Manickavasagan H, Kumar A. Su1341 Efficacy of Celiac Plexus Block in Chronic Pancreatitis-A Systematic Review. *Gastrointestinal Endoscopy.* 2017;85(5):AB341-2.

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Question 40

A 56-year-old man with alcohol-related chronic calcific pancreatitis presents with chronic abdominal pain. His pain regimen includes oxycodone 5 mg orally three times daily and gabapentin. On this regimen, he reports 5/10 to 6/10 upper abdominal pain. Pain is frequently postprandial and occasionally associated with nausea and emesis. He has been admitted to the hospital for pain control twice in the past year. He has quit alcohol use but continues to smoke a half pack of cigarettes daily. He has no other significant medical problems. Computed tomography is performed and reveals calcifications in the head of pancreas with dilation of the upstream pancreatic duct measuring up to 10 mm (Figures A and B). Endoscopic retrograde cholangiopancreatography with lithotripsy is performed, which only temporarily improves his pain.

What would you recommend as the next best option for duct decompression and pain control?



Figure A



Figure B

- A. Celiac plexus block
- B. Endoscopic retrograde cholangiopancreatography with stent placement
- C. Endoscopic ultrasound-guided pancreatic drainage
- D. Surgical duct decompression
- E. Total pancreatectomy with islet autotransplantation

CORRECT ANSWER: D

RATIONALE

In patients with chronic pancreatitis with symptomatic large duct obstruction of the pancreatic duct, establishing ductal drainage can improve pain. This can be performed by endoscopic and surgical drainage procedures. Surgical drainage appears to be more effective and durable than endoscopic drainage procedures. Especially in medically fit patients who fail first-line endoscopic approach to ductal decompression, surgical management with approaches such as lateral pancreaticojejunostomy should be recommended. Endoscopic ultrasound-guided pancreatic drainage is a relatively novel and promising intervention, but it is not widely available and long-term efficacy and safety data are required to confirm benefits. Celiac plexus block and total pancreatectomy with islet autotransplantation are options for pain in patients with nonobstructive disease.

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on Pain in Patients With Chronic Pancreatitis: The ESCAPE Randomized Clinical Trial. *JAMA*. 2020;323(3):237-247. doi:10.1001/jama.2019.20967

Question 41

A 68-year-old woman with long-standing hereditary chronic pancreatitis is seen for follow-up. She has been maintained on pancreatic enzyme supplementation for several years for steatorrhea related to exocrine pancreatic insufficiency. She reports a recent diagnosis of diabetes mellitus treated with metformin. She also reports a 10-pound weight loss over the past 3 months; she currently weighs 68 kg with a body mass index of 25 kg/m². She has multiple family members with pancreatitis and has previously tested positive for a mutation in the *PRSS1* gene. Her past medical history is significant for hypertension, osteoarthritis, gastrointestinal esophageal reflux disease, and diverticulosis. Her physical examination is unremarkable.

What do you recommend next for management?

- A. Bone density scan
- B. Computed tomography of abdomen
- C. Endoscopic retrograde cholangiopancreatography
- D. Pancreatic enzyme dose increase
- E. Surgical referral

CORRECT ANSWER: B

RATIONALE

Patients with chronic pancreatitis are at risk of pancreatic cancer, with the highest risk in those with hereditary and tropical pancreatitis. In these patients, unexplained weight loss, new-onset diabetes, and other clinical features such as pain pattern change and new-onset depression can suggest development of pancreatic cancer. They need further evaluation with cross-sectional imaging (computed tomography or magnetic resonance

imaging) or endoscopic ultrasound to evaluate for pancreatic cancer. In patients with new-onset diabetes, risk factors for pancreatic cancer are age 65 years and older, heavy smoking, nonobese status at diagnosis, and history of chronic pancreatitis. Bone density scan and pancreatic enzyme dose changes would not help rule out pancreatic cancer. Endoscopic retrograde cholangiopancreatography would only be helpful if there was duct disruption. Prior to surgery referral, evaluation with cross sectional imaging would be indicated.

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Question 42

A 35-year-old woman presents for evaluation of chronic pancreatitis. She has had 3 hospital admissions for acute-on-chronic pancreatitis in the past 2 years and has chronic abdominal pain between episodes. Computed tomography during hospitalizations showed evidence of pancreatic calcifications and ductal irregularity. The patient denies weight loss and bowel habit changes. She denies tobacco and alcohol use. She is adopted and denies knowledge of family history of pancreatic diseases. She is on tramadol and gabapentin for pain. Her laboratory tests reveal normal calcium, triglyceride, and IgG subclass levels.

What would you recommend as the next best step in management?

- A. Endoscopic ultrasound and fine-needle biopsy
- B. Fecal elastase test
- C. Genetic testing
- D. Secretin-enhanced magnetic resonance cholangiopancreatography
- E. Sweat chloride test

CORRECT ANSWER: C

RATIONALE

Genetic testing is indicated in patients with chronic pancreatitis without a clear etiology, especially in those who are young, have a family history of chronic pancreatitis, or have syndromic features suggestive of a genetic predisposition. This information can direct further management (eg, total pancreatectomy with islet autotransplantation) and help to determine prognosis. This patient's computed tomography scan confirms diagnosis of chronic pancreatitis; hence, obtaining histology via fine-needle biopsy or performing secretin-enhanced magnetic resonance cholangiopancreatography is not required for diagnostic purpose. Fecal elastase testing can help with diagnosis of exocrine pancreatic insufficiency but is not immediately indicated here in the absence of malabsorption symptoms. Sweat chloride testing can help with disease diagnosis if genetic testing shows *CFTR* gene mutations.

REFERENCE

Gardner TB, Adler DG, Forsmark CE, Sauer BG, Taylor JR, Whitcomb DC. ACG Clinical Guideline: Chronic Pancreatitis. *Am J Gastroenterol*. 2020;115(3):322-339. doi:10.14309/ajg.0000000000000535

Question 43

A 77-year-old man presents for evaluation of a large mass in the body and tail region of the pancreas and abdominal pain. He undergoes magnetic resonance imaging, which shows a 5.8-cm mass in the body and tail of the pancreas, described as a T2 hypointense, enhancing lesion. A T2 hypoin-

tense rim is seen with a hypoattenuating halo on postcontrast images (Figure A). Laboratory tests reveal a carbohydrate antigen 19-9 level of 18 U/mL (reference range, 0-37 U/mL and IgG4 level of 519 mg/dL (reference range, 4-135 mg/dL). An endoscopic ultrasound with fine-needle biopsy is performed. Pathology shows a prominent fibroinflammatory process (Figure B). Immunostaining for IgG4 demonstrated infiltration of IgG4-positive plasma cells (>10 cells in this field; Figure C).

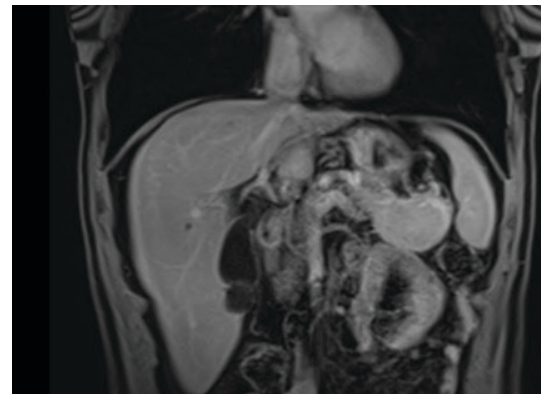


Figure A

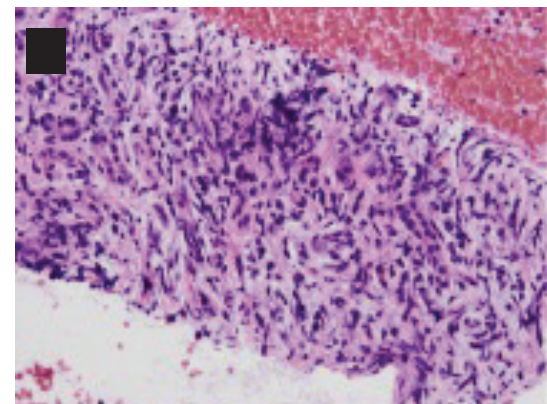


Figure B

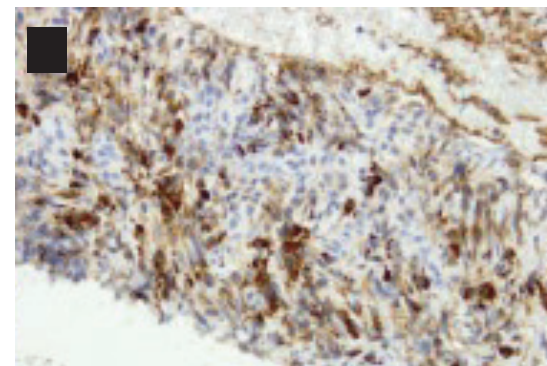


Figure C

What is the diagnosis?

- A. Chronic pancreatitis
- B. Pancreatic adenocarcinoma
- C. Pancreatic lymphoma
- D. Type 1 autoimmune pancreatitis
- E. Type 2 autoimmune pancreatitis

CORRECT ANSWER: D

RATIONALE

This patient's presentation and pathology is diagnostic of type 1 autoimmune pancreatitis (AIP). Type 1 AIP is typically seen in males in the sixth to seventh decade of life, with elevation of serum IgG4 level. Pathology shows lymphoplasmacytic sclerosing pancreatitis or greater than 10 IgG4-positive cells with at least 2 of the following: periductal lymphoplasmacytic infiltrate, obliterative phlebitis, and/or swirling collagen fibers (storiform fibrosis).

In contrast, type 2 AIP is seen in younger age groups with equal prevalence in males and females. Type 2 AIP can be associated with inflammatory bowel disease. IgG4 level is normal or mildly elevated. Pathology shows a granulocytic epithelial lesion in the pancreatic duct with minimal IgG4-positive cells in the pancreatic parenchyma. The pathology in this case is not consistent with a neoplastic process.

REFERENCE

Hart PA, Zen Y, Chari ST. Recent Advances in Autoimmune Pancreatitis. *Gastroenterology*. 2015;149(1):39-51. doi:10.1053/j.gastro.2015.03.010

Question 44

A 35-year-old woman with Crohn's disease in remission on infliximab and azathioprine is admitted to the hospital with nausea, emesis, and upper abdominal pain radiating to the back.

Laboratory tests reveal results shown below.

Computed tomography reveals a diffusely enlarged, "sausage like" pancreas with a hypodense rim (Figure A). An IgG4 level is subsequently obtained and is noted to be 150 mg/dL (reference range, 4-135 mg/dL).

What is the next best step in management of this patient's pancreatitis?



Figure A

- A. Start mycophenolate
- B. Start rituximab
- C. Start steroids
- D. Stop azathioprine
- E. Switch infliximab to adalimumab

CORRECT ANSWER: C

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	120	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	45	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	35	10-40
Bilirubin, serum (total), mg/dL	1.2	0.3-1.0
Leukocyte (WBC) count, cells/ μ L	10,000	4000-11,000
Lipase, serum, U/L	500	10-140

RATIONALE

This patient likely has imaging and serologic evidence of autoimmune pancreatitis (AIP). Based on her age, IgG4 level, and history of inflammatory bowel disease, she most likely has type 2 autoimmune pancreatitis. Histology can be obtained via endoscopic ultrasound to support diagnosis, but initiating steroids and assessing for response can be considered as a diagnostic and therapeutic measure (histology, imaging, serology, other organ involvement, and response to therapy criteria). Mycophenolate and rituximab are not first-line therapeutic agents for AIP. Drug-induced pancreatitis can be seen with azathioprine.

However, the clinical picture here supports AIP; hence, discontinuation of azathioprine is not indicated. Mycophenolate and rituximab are not first-line therapeutic agents for AIP.

REFERENCES

Akshintala VS, Singh VK. Management of Autoimmune Pancreatitis. *Clin Gastroenterol Hepatol*. 2019;17(10):1937-1939. doi:10.1016/j.cgh.2019.04.052

Hart PA, Zen Y, Chari ST. Recent Advances in Autoimmune Pancreatitis. *Gastroenterology*. 2015;149(1):39-51. doi:10.1053/j.gastro.2015.03.010

Question 45

Screening for pancreatic cancer is recommended for individuals with which of the following conditions?

- A. Chronic pancreatitis
- B. Family with PTEN mutation
- C. First-degree relative with pancreatic cancer at age <60 years
- D. Multiple endocrine neoplasia 1 syndrome
- E. Peutz-Jeghers syndrome

CORRECT ANSWER: E

RATIONALE

The International Cancer of the Pancreas Consortium consensus recommends screening for pancreatic cancer for the following individuals: all patients with Peutz-Jeghers syndrome; all carriers of a germline *CDKN2A* mutation; carriers of a germline *BRCA2*, *BRCA1*, *PALB2*, *ATM*, *MLH1*, *MSH2*, or *MSH6* gene mutation with at least 1 affected first-degree blood relative; and, individuals who have at least 1 first-degree relative with pancreatic cancer who in turn also has a first-degree relative with pancreatic cancer (familial pancreatic cancer kindred). The other answer choices are not conditions for which pancreatic cancer screening is recommended.

REFERENCE

Goggins M, Overbeek KA, Brand R, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. *Gut*. 2020;69(1):7-17. doi:10.1136/gutjnl-2019-319352

Question 46

A 46-year-old man with a family history of pancreatic cancer is referred to you for recommendations. He reports that his mother died of pancreatic cancer in her 60s and that his maternal aunt died from pancreatic cancer in her 50s. There is no history of breast or colon cancer on that side of his family. He denies history of pancreatitis, abdominal pain, and unintentional weight loss. What do you recommend next?

- A. Carcinoembryonic antigen and carbohydrate 19-9 tests
- B. Endoscopic ultrasound (EUS) with/without fine-needle aspiration
- C. Genetic counseling and germline genetic testing
- D. Magnetic resonance imaging (MRI)/MR cholangiopancreatography (MRCP)
- E. Pancreatic protocol computed tomography (CT)

CORRECT ANSWER: C**RATIONALE**

This patient belongs to a family with 2 or more first-degree relatives who do not have pre-disposition for a known pancreatic cancer-associated hereditary syndrome and meet criteria for familial pancreatic cancer (FPC). These high-risk FPC kindreds should be referred for genetic counseling and germline genetic testing. The International Cancer of the Pancreas Consortium consensus recommendations are for the FPC kindreds to be enrolled in a long-term screening program for pancreatic cancer, which includes a baseline EUS, MRI/MRCP, and fasting blood glucose and/or hemoglobin A_{1c} test. Subsequently, annual examinations alternating MRI and EUS are recommended. Tumor markers, fine-needle aspiration, and CT are recommended if concerning features are found on MRI or EUS.

REFERENCE

Goggins M, Overbeek KA, Brand R, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. *Gut*. 2020;69(1):7-17. doi:10.1136/gutjnl-2019-319352

Question 47

A 36-year-old man with a history of cystic fibrosis (CF) presents to his primary care provider. Which of the following is the most common pancreatic complication for this patient?

- A. Acute pancreatitis
- B. Chronic pancreatitis
- C. CF-related diabetes

- D. Exocrine pancreatic insufficiency
- E. Pancreatic cancer

CORRECT ANSWER: D**RATIONALE**

Pancreatic disease is an important manifestation of CF. Exocrine pancreatic insufficiency is the most common gastrointestinal manifestation of CF, affecting 85% to 90% of patients with CF. Acute and chronic pancreatitis and diabetes are less common pancreatic complications of CF. Patients with CF are at increased risk of pancreatic cancer compared with the general population.

REFERENCE

Whitcomb DC, Lowe ME. Genetic Disorders of the Pancreas and Pancreatic Disorders in Childhood. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*, 11th ed. Elsevier, Inc; 2020:862-892.

Question 48

A 60-year-old man with hypertension, diabetes mellitus, and obesity presented with chronic abdominal pain and was found to have a 2-cm mass in the head of the pancreas. At the time of presentation his total bilirubin level was normal. Endoscopic ultrasound with fine-needle aspiration confirmed pancreatic adenocarcinoma. While awaiting consultation with surgical oncology, the patient develops jaundice, pale stools, and dark urine.

Laboratory tests reveal the following results shown below.

Computed tomography of the abdomen is performed and shows a 2.5-cm heterogeneously

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	600	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	100	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	90	10-40
Bilirubin, serum (total), mg/dL	5.7	0.3-1.0
Leukocyte (WBC) count, cells/ μ L	7000	4000-11,000

enhancing mass centered within the head of the pancreas. Diffuse intrahepatic and extra hepatic biliary dilation was seen upstream to the mass. Adjacent vasculature is uninvolved.

No lymphadenopathy is seen. No evidence of distant metastatic disease is present on computed tomography.

What is the next best step in management of this patient?

- A. Endoscopic retrograde cholangiopancreatography with stent placement
- B. Neoadjuvant chemotherapy
- C. Pancreaticoduodenectomy
- D. Percutaneous biliary drainage
- E. Positron emission tomography/computed tomography

CORRECT ANSWER: C

RATIONALE
This patient has imaging evidence of localized resectable cancer of the pancreas without regional lymphadenopathy, involvement of local blood vessels, or distant metastasis. As such, the patient can proceed to have surgical resection. Preoperative biliary drainage has not been shown to improve outcomes in patients with obstructive jaundice and may be associated with shorter survival. As such, routine preoperative biliary drainage is not required in patients who have resectable disease on imaging except in those who have cholangitis, severe jaundice (>15 mg/dL) or expected delays in surgery. Hence, endoscopic retrograde cholangiopancreatography with stent placement or percutaneous drainage are not required. At this time, rou-

tine neoadjuvant chemotherapy is not indicated in patients with resectable disease on imaging. The positron emission tomography/computed tomography is not needed with the information already obtained by the computed tomography.

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Barauskas G, Urbonas K, Smailyte G, Pranys D, Pundzius J, Gulbinas A. Preoperative Endoscopic Biliary Drainage May Negatively Impact Survival Following Pancreatoduodenectomy for Ampullary Cancer. *Dig Surg.* 2016;33(6):462-469. doi:10.1159/000445777

Dumonceau JM, Tringali A, Papanikolaou IS, et al. Endoscopic biliary stenting: indications, choice of stents, and results: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline - Updated October 2017. *Endoscopy.* 2018;50(9):910-930. doi:10.1055/a-0659-9864

Question 49
A 67-year-old man is admitted to the hospital with jaundice, dark urine, and chalky stool. He reports a 15-pound weight loss in the past 2 months.

Laboratory tests show the following results shown at the bottom of the page.

Computed tomography is performed and reveals a 4.2-cm mass in the head and uncinate process of the pancreas with upstream extra- and intrahepatic biliary dilation. The mass was noted to have less than 180-degree short segment contact with the superior mesenteric vein.

What is the next best step in this patient’s management?

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	550	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	120	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	90	10-40
Bilirubin, serum (total), mg/dL	10	0.3-1.0

- A. Endoscopic retrograde cholangiopancreatography (ERCP) with stent placement
- B. Endoscopic ultrasound (EUS) with fine-needle aspirate (FNA) or biopsy (FNB)
- C. EUS with FNA/FNB and ERCP
- D. Neoadjuvant chemotherapy
- E. Pancreaticoduodenectomy

CORRECT ANSWER: C

RATIONALE

Locally advanced pancreatic cancer can involve adjacent vasculature (superior mesenteric vein, portal vein, superior mesenteric artery, celiac trunk, common hepatic artery, among others). Based on the vessel involved and degree of contact, these tumors are classified as borderline resectable or locally advanced unresectable at presentation. This patient likely has borderline resectable pancreatic cancer based on the fact that only a short segment of the superior mesenteric artery is involved (<180 degrees of contact). The current approach to management of borderline resectable pancreatic cancer is administration of neoadjuvant chemotherapy followed by surgical resection. The next step in this patient's management would be to obtain tissue diagnosis by EUS with FNA or FNB and establishing biliary drainage via ERCP and stent placement given the expected delay in surgery during treatment with neoadjuvant chemotherapy. The extrahepatic and intrahepatic ductal dilation with cholestatic obstruction would favor intervention with ERCP in this case as a first step.

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Jutric Z, Melstrom LG. New Treatment Options and Management Considerations in Borderline Resectable Pancreatic Cancer. *Oncology (Williston Park)*. 2017;31(6):443-452.

Park W, Chawla A, O'Reilly EM. Pancreatic Cancer: A Review. *JAMA*. 2021;326(9):851-862. doi:10.1001/jama.2021.13027

Question 50

A 75-year-old man with hypertension, obstructive sleep apnea on continuous positive airway pressure, congestive heart failure, and newly diagnosed metastatic pancreatic cancer underwent endoscopic ultrasound and fine-needle biopsy for tissue diagnosis and endoscopic retrograde cholangiopancreatography with self-expandable metal stent placement for palliation of biliary obstruction. He is admitted to the hospital with persistent abdominal pain, nausea, emesis, and dehydration.

Computed tomography reveals duodenal obstruction and significant distention of the stomach with air-fluid level. An esophagogastroduodenoscopy is performed and reveals high-grade, malignant-appearing stenosis in the second portion of the duodenum (Figure A).

What is the next best step for palliation of his gastric outlet obstruction?

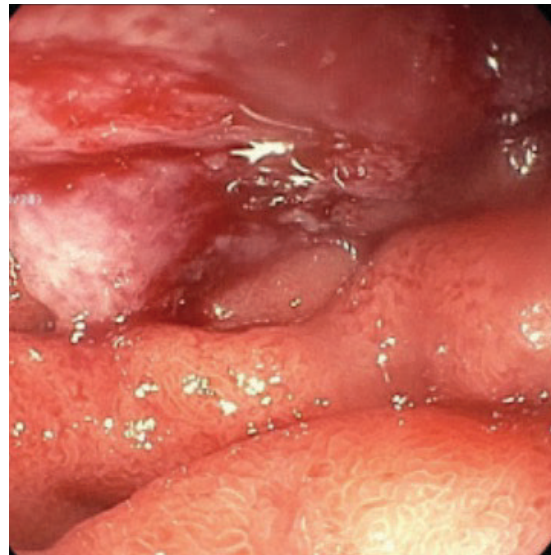


Figure A

- A. Celiac plexus neurolysis
- B. Chemoradiation
- C. Duodenal stent placement
- D. Endoscopic gastrojejunostomy
- E. Surgical bypass

CORRECT ANSWER: C

RATIONALE

Duodenal stent placement and endoscopic and surgical gastrojejunostomy are all options for management of malignant gastric outlet obstruction. Endoscopic stent placement has been shown to provide rapid relief of symptoms with shorter hospital stays. Surgical bypass has been shown to have better long-term outcomes and less need for reintervention. However, in patients with poor functional status or short life expectancy, as in those with metastatic pancreatic cancer, duodenal stent placement is the best strategy. Recent studies show that endoscopic ultrasound-guided gastroenterostomy is a safe and effective option in experienced hands. However, the technique is not well standardized and is limited to a few centers. Celiac plexus neurolysis is an option for pain management in pancreatic cancer but not for obstruction. Chemoradiation is unlikely to provide effective palliation of duodenal obstruction.

REFERENCE

Troncone E, Fugazza A, Cappello A, et al. Malignant gastric outlet obstruction: Which is the best therapeutic option?. *World J Gastroenterol*. 2020;26(16):1847-1860. doi:10.3748/wjg.v26.i16.1847

CHAPTER 4

Diseases of the biliary tract

Daniel Strand, MD and Dushant Uppal, MD

Question 1

A 43-year-old woman presents to her local emergency department with recurrent right upper quadrant (RUQ) pain of 6 hours duration. Her vital signs reveal tachycardia (110 bpm), with normal blood pressure and temperature. On examination, she has mild tenderness in the RUQ without rebound, guarding, or rigidity.

Laboratory testing reveals results shown below.

Her complete blood count and basic metabolic profile are unremarkable. RUQ ultrasound then demonstrates a 10-mm diameter common bile duct, cholelithiasis without gallbladder wall thickening, normal Doppler flow, and nonvisualization of the pancreatic head due to interposing air.

What is the most appropriate next step in management?

- A. Abdominal magnetic resonance cholangiopancreatography
- B. Laparoscopic cholecystectomy referral
- C. Endoscopic retrograde cholangiopancreatography
- D. Pancreas protocol computed tomography
- E. Serial liver biochemistries and serologic testing

CORRECT ANSWER: A**RATIONALE**

The patient presents with classic symptoms of biliary colic, in the absence of physical signs of cholecystitis, and in the presence of abnormal liver biochemistries and bile duct dilation. Although this presentation is highly compatible with a common bile duct stone, the laboratory results presented have specificity of only 85% for stone recovery during endoscopic retrograde cholangiography. To avoid unnecessary risk, patients should undergo a risk-stratifying test (either magnetic resonance imaging or endoscopic ultrasound) unless a stone is seen on ultrasound, clinical presentation is concerning for acute bacterial cholangitis, or both a dilated bile duct (10 mm) and total bilirubin level greater than 4 g/dL are detected. Laparoscopic cholecystectomy, while eventually indicated, would not effectively diagnose or address the likely common bile duct stone (especially without intraoperative cholangiography). Endoscopic retrograde cholangiopancreatography is indicated for stone retrieval but would be performed unnecessarily up to 15% of the time based upon the specific information provided by the question stem. Computed tomography is not sufficiently sensitive for detection of common bile duct stones and would likely demonstrate only

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	100	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	195	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	120	10-40
Bilirubin, total, serum, mg/dL	2.4	0.3-1.0

bile duct dilation, which is already seen on the patient’s RUQ ultrasound. Serial liver biochemistries, while helpful in following the patient’s course, are also unhelpful in establishing a concrete etiology – in this case identification or nonidentification of a bile duct stone.

REFERENCES

Buxbaum JL, Fehmi SMA, Sultan S, et al. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. *Gastrointest Endosc.* 2019; 89(6):1075-1105.e15. doi:10.1016/J.GIE.2018.10.001

He H, Tan C, Wu J, et al. Accuracy of ASGE high-risk criteria in evaluation of patients with suspected common bile duct stones. *Gastrointest Endosc.* 2017; 86(3):525-532. doi:10.1016/J.GIE.2017.01.039.

Question 2

A 52-year-old man is referred to your office for evaluation of elevated liver enzymes. On interview, he reports a 2- to 3-month history of vague right upper quadrant discomfort, intermittent pruritus, and xerostomia. He has previously experienced 2 remote episodes of clinically mild, idiopathic pancreatitis. On examination, he has normal vital signs, minimal abdominal distension, and enlarged submandibular salivary glands. Basic Laboratory testing reveals the following results shown below.

His complete blood count and basic metabolic panel are unremarkable. Subsequent magnetic resonance imaging of the abdomen reveals diffuse, continuous thickening and enhancement of the extrahepatic bile duct (3-mm diameter). Magnetic resonance cholangiopancreatography (MRCP) and

T2 sequences reveal a funnel-shaped narrowing of the proximal common hepatic duct with mildly dilated intrahepatic ducts. Multiple low-density lesions are also noted in the left renal cortex, as shown in the image below.



IMAGE COURTESY OF DANIEL STRAND, MD.

What is the most appropriate next step in management?

- A. Endoscopic retrograde cholangiopancreatography with uncovered metal stent placement
- B. Glucocorticoid treatment
- C. Intravenous rituximab infusion
- D. Percutaneous liver biopsy
- E. Right upper quadrant ultrasound with Doppler

CORRECT ANSWER: B

RATIONALE

This patient presents with signs and symptoms of systemic IgG4-related disease (IgG4-RD) involving multiple organ systems. Specifically, he has sialadenitis (Mikulicz disease), renal involvement (tubulointerstitial nephritis), and IgG4-related cholangitis. His history of idiopathic pancreatitis

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	220	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	45	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	65	10-40
Bilirubin, total, serum, mg/dL	1.6	0.3-1.0

suggests metachronous type 1 autoimmune pancreatitis. The available information is sufficient to establish IgG4-RD, which includes multisystem involvement and highly specific imaging findings. Treatment is indicated for all symptomatic patients with extrapancreatic disease, and first-line therapy is glucocorticoids. Although endoscopic retrograde cholangiopancreatography may be indicated for symptom relief in adult patients with IgG4-RD, placement of an uncovered metal stent is expressly contraindicated as this is not removable. Placement of uncovered self-expanding metal stents should be reserved for patients with malignant biliary obstruction. An additional right upper quadrant ultrasound would not add additional information to the imaging studies previously described. A percutaneous liver biopsy is potentially useful for diagnosis of a mass lesion or in uncovering an overlap syndrome with autoimmune hepatitis, though this is rare. Liver biopsy specimens in IgG4-related cholangiopathy alone are often unreliable and interpreted as *reactive*. Rituximab should be considered for patients who are resistant or intolerant of high-dose glucocorticoids. It is the only drug, apart from steroids, that has been shown to induce remission in IgG4-RD. Corticosteroids, however, are first-line treatment.

REFERENCES

Löhr JM, Beuers U, Vujasinovic M, et al. European Guideline on IgG4-related digestive disease - UEG and SGF evidence-based recommendations. *United European Gastroenterol J*. 2020;8(6):637-666. doi:10.1177/2050640620934911

Wallace ZS, Naden RP, Chari S, et al. The 2019 American College of Rheumatology/European

League Against Rheumatism Classification Criteria for IgG4-Related Disease. *Arthritis Rheumatol*. 2020;72(1):7-19. doi:10.1002/art.41120

Question 3

A 61-year-old man without known liver disease presents for evaluation of new-onset jaundice and pruritis. Laboratory tests reveal the following results shown below.

Laboratory tests also show viral hepatitis serologies consistent with prior vaccination for hepatitis A and B viruses. Contrasted magnetic resonance imaging demonstrates a 28-mm mass lesion, with delayed enhancement, originating in the right posterior hepatic hilum. Obstruction of the hepatic bifurcation, including independent strictures of the right anterior and right posterior hepatic ducts, are noted. The right hepatic artery and portal vein are encased, but the left vasculature is patent.

The left liver is not atrophic, but the volume is relatively small (20%). What is the most appropriate next step in management?

- A. Chemotherapy
- B. Endoscopic retrograde cholangiopancreatography with brush cytology and plastic stent placement into 2 or more liver sectors
- C. Endoscopic ultrasound with fine-needle aspiration of lesion for tissue acquisition
- D. Percutaneous biopsy of lesion for tissue acquisition
- E. Right portal vein embolization followed by right hepatectomy

Laboratory Test	Result	Reference Range
Alpha-fetoprotein, serum, ng/mL	5	<10
Alkaline phosphatase, serum, U/L	560	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	210	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	182	10-40
Bilirubin (total), serum, mg/dL	12	0.3-1.0
Carbohydrate antigen 19-9, serum, U/mL	340	0-37
Carcinoembryonic antigen, plasma, ng/mL	4	<2.5

CORRECT ANSWER: B

RATIONALE

The patient presents with clinical, laboratory, and radiographic features of cholangiocarcinoma. In addition, the patient is symptomatic and has significant pruritis and obstructive jaundice. The first step in confirmation of this diagnosis is the acquisition of a tissue sample; of the available choices, endoscopic retrograde cholangiopancreatography with brush cytology and plastic stent placement into 2 or more liver sectors is the only available choice that would avoid a transperitoneal approach. Transcutaneous (choice D) and endoscopic ultrasound-directed (choice C) approaches to sampling of a hilar mass lesion may have high sensitivity for diagnosis of cholangiocarcinoma but have been associated with an increased risk of percutaneous or peritoneal metastasis. The location of the mass at the hilum also increases the risk of percutaneous biopsy. While chemotherapy (Choice A) and preparatory intervention(s) before surgery (Choice E) are reasonable treatment options for this patient, the decision to pursue these should follow an attempt at cytologic diagnosis and relief of symptomatic cholestasis.

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- El Chafic AH, Dewitt J, Leblanc JK, et al. Impact of preoperative endoscopic ultrasound-guided fine needle aspiration on postoperative recurrence and survival in cholangiocarcinoma patients. *Endoscopy*. 2013;45(11):883-889. doi:10.1055/s-0033-1344760
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- Qumseya BJ, Jamil LH, Elmunzer BJ, et al. ASGE guideline on the role of endoscopy in the management of malignant hilar obstruction. *Gastrointest Endosc*. 2021;94(2):222-234.e22. doi:10.1016/j.gie.2020.12.035

Téllez-Ávila FI, Bernal-Méndez AR, Guerrero-Vázquez CG, Martínez-Lozano JA, Ramírez-Luna MÁ. Diagnostic yield of EUS-guided tissue acquisition as a first-line approach in patients with suspected hilar cholangiocarcinoma. *Am J Gastroenterol*. 2014;109(8):1294-1296. doi:10.1038/ajg.2014.169

Question 4

A 47-year-old woman is evaluated in the emergency department 4 days after elective laparoscopic cholecystectomy for symptomatic cholelithiasis. On arrival, she has significant right upper quadrant abdominal pain, nausea, and a fever. Vital signs demonstrate a normal blood pressure but tachycardia (heart rate, 105 bpm). On examination, she exhibits rebound tenderness and voluntary guarding on palpation of the right abdomen. Laboratory tests demonstrate normal serum total bilirubin, aspartate aminotransferase, and alanine aminotransferase levels but a leukocyte count of 18,000 cells/ μ L (reference range, 4000–11,000 cells/ μ L). During observation and initial work-up, she is noted to have an episode of rigors. Cross-sectional imaging in the form of a contrasted computed tomography scan of the abdomen is performed, which revealed a 6-cm partially loculated fluid collection in the gallbladder fossa.

What is the most appropriate next step in management?

- Endoscopic retrograde cholangiopancreatography with biliary sphincterotomy
- Endoscopic retrograde cholangiopancreatography with plastic stent placement
- Hepatobiliary scintigraphy scan
- Laparotomy with hepaticojejunal biliary anastomosis
- Percutaneous catheter drainage of subhepatic fluid collection

CORRECT ANSWER: E

RATIONALE

The patient presents with a postoperative bile duct leak, complicated by evidence of infection, which is suggested by the presence of fever and rigors. Given the presence of a fluid collection and multiple systemic inflammatory response syndrome, control of the potential infection source is the next most appropriate step. Endoscopic retrograde cholangiopancreatography with sphincterotomy or stent placement may be effective management to resolve a postoperative bile leak but will not address the symptomatic (and likely infected) fluid collection. Additionally, although data support the use of sphincterotomy alone for low-grade bile leaks, little definitive evidence is available to suggest that this strategy is sufficient for high-grade injuries. Hepatobiliary scintigraphy scan, although potentially useful in diagnosis of a bile leak, is an unnecessary step that may cause a significant delay in definitive management. A laparotomy with hepaticojejunal biliary anastomosis and its accompanying risks would be too invasive for the patient who will likely respond to more conservative measures.

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Ahmad F, Saunders RN, Lloyd GM, Lloyd DM, Robertson GS. An algorithm for the management of bile leak following laparoscopic cholecystectomy. *Ann R Coll Surg Engl*. 2007;89(1):51-56. doi:10.1308/003588407X160864

Núñez D Jr, Becerra JL, Martin LC. Subhepatic collections complicating laparoscopic cholecystectomy: percutaneous management. *Abdom Imaging*. 1994;19(3):248-250. doi:10.1007/BF00203518

Rainio M, Lindström O, Udd M, Haapamäki C, Nordin A, Kylänpää L. Endoscopic Therapy of Biliary Injury After Cholecystectomy. *Dig Dis Sci*. 2018;63(2):474-480. doi:10.1007/s10620-017-4768-7

Question 5

A 57-year-old man patient is seen in consulta-

tion 18 days after right-lobe, living-donor liver transplantation. On postoperative day 4, he was found to have symptomatic hepatic artery narrowing, which required placement of an endovascular stent via angiography. He now presents with increased output from a surgical Jackson-Pratt drain, which has visibly changed in character from serosanguinous to tawny-green. During endoscopic retrograde cholangiopancreatography (ERCP), a sequential series of cholangiograms without balloon occlusion is performed and these are shown below. Additionally, wire access into the proximal liver ducts is technically challenging due to repeated looping below the transplant anastomosis. Instrument passage is feasible, but passage of an extraction balloon across the transplant anastomosis is met with significant resistance.

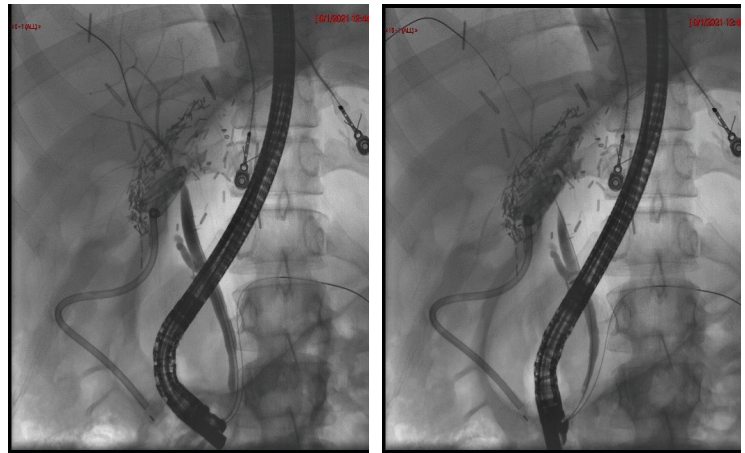


IMAGE COURTESY OF DANIEL STRAND, MD.

What is the most appropriate next step in management?

- A. Biliary sphincterotomy alone
- B. Biliary sphincterotomy and balloon dilation of transplant anastomosis
- C. Biliary sphincterotomy and placement of a plastic stent
- D. No biliary sphincterotomy, proceed with percutaneous transhepatic biliary drainage
- E. No biliary sphincterotomy and proceed with listing for retransplantation

CORRECT ANSWER: C

RATIONALE

The patient presents with a posttransplant biliary stricture and accompanying leak, resulting from early postoperative ischemia in the setting of poor hepatic artery perfusion. Biliary strictures are a common complication of hepatic artery stenosis, occurring in up to 40% of patients with this pathology. Although the ERCP and drain output indicate a bile leak, this has occurred in the setting of significant anastomotic narrowing. Transampullary plastic stent placement would affect treatment of both the leak and the observed stricture. Biliary sphincterotomy alone, would not be appropriate in this setting due the presence of a significant untreated stricture (although it may be sufficient for other forms of low-grade bile leaks). Balloon dilation, additionally, would not be appropriate in the immediate treatment of a postoperative bile leak. Percutaneous transhepatic biliary drainage can be an effective rescue management strategy if ERCP is unsuccessful, particularly if the strictured anastomosis cannot be crossed. Hepatic artery thrombosis is a risk factor for significant graft-loss or liver failure after transplantation, but no indication of liver failure is provided in the clinical vignette.

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Question 6

A 48-year-old woman is referred for upper endoscopy to assess persistent heartburn despite antisecretory therapy with omeprazole. Although the remainder of her examination is normal, she is found to have an enlarged and atypical-appearing major papilla. Endoscopic images are shown below.

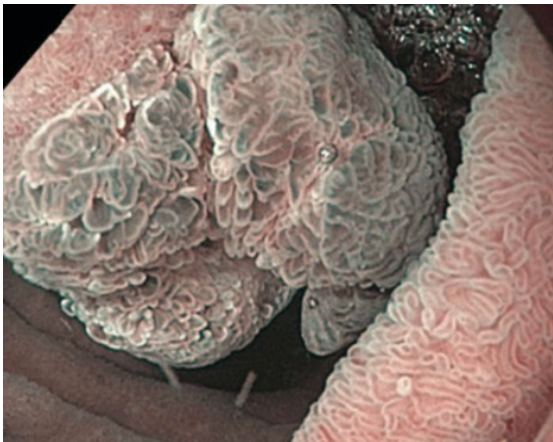
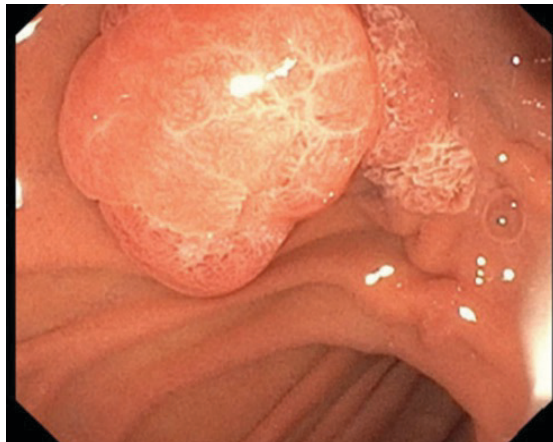


IMAGE COURTESY OF DANIEL STRAND, MD.

Review of her medical record demonstrates recent liver biochemistry levels are below.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	72	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	19	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	25	10-40
Bilirubin, total, serum, mg/dL	0.8	0.3-1.0

She is otherwise healthy, on no prescription medications, and has no family history of colorectal cancer.

What is the most appropriate next step in management?

- A. Cold forceps biopsies
- B. Endoscopic resection via ampullectomy
- C. Endoscopic surveillance of the ampullary lesion
- D. Pancreaticoduodenectomy
- E. Surgical ampullectomy

CORRECT ANSWER: A

RATIONALE

The patient presents with a visible ampullary lesion that is morphologically consistent with an ampullary adenoma. The first step in management of these lesions is careful visual assessment, followed by ampullary biopsy. Biopsy is essential before intervention, as visual characteristics of an ampullary adenoma may be difficult or impossible to distinguish from other, nonadenomatous lesions of the major papilla, such as carcinoid tumors or paragangliomas. Additionally, ampullary carcinoma may not be distinguishable from a noninvasive lesion by inspection alone. Both endoscopic surveillance and resection may be appropriate for patients with ampullary adenomas; however, without histopathologic confirmation of a diagnosis, the determination regarding resection or surveillance would be premature. Surgical management of ampullary adenomas (pancreaticoduodenectomy or surgical ampullectomy) has been historically commonplace but can be associated with considerable morbidity and should be reserved for lesions that are inappropriate for endoscopic management, such as those with

invasive carcinoma that involves the pancreaticobiliary axis.

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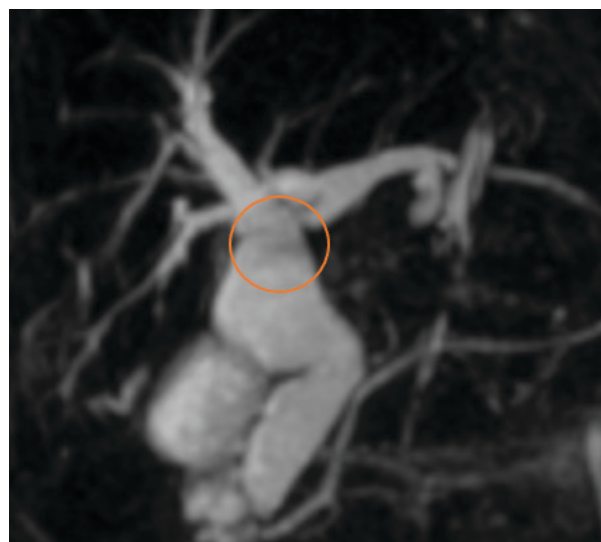
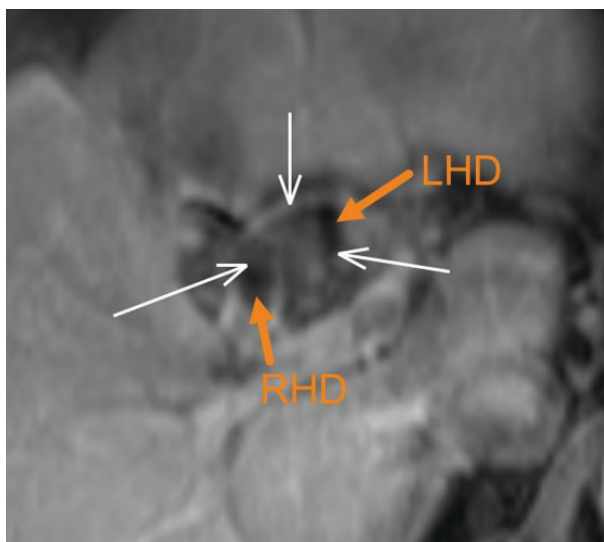
Question 7

A 73-year-old woman is referred in consultation after cross-sectional imaging, performed after a minor traffic accident, demonstrated previously unknown dilation of the biliary tract. Although she recovered well from the incident, she now reports a 10-pound unintentional weight loss and fatigue over the previous 3 months.

A complete blood count is unremarkable, and her liver biochemistry levels are below.

Contrasted magnetic resonance imaging of the abdomen is performed, and images are presented on the following page.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	180	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	37	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	45	10-40
Bilirubin, total, serum, mg/dL	0.8	0.3-1.0



Subsequently, an endoscopic retrograde cholangiopancreatography (ERCP) with cholangioscopy is performed, revealing a papillary, mucin-covered growth that involves the common and left hepatic ducts while sparing the right biliary system. Histology from cholangioscopic biopsies demonstrate an adenocarcinoma with underlying papillary proliferation and a fibrovascular core.

Which of the following interventions is associated with the clearest overall survival benefit?

- A. ERCP with bilateral hilar stent placement alone
- B. ERCP with photodynamic therapy and stent placement
- C. External beam radiotherapy with chemosensitization
- D. Gemcitabine and platinum-based chemotherapy
- E. Surgical bile duct excision, hilar dissection, and left hepatic lobectomy

CORRECT ANSWER: E

RATIONALE

The patient presents with a biliary carcinoma, arising from an intraductal papillary neoplasm of the bile duct (IPNB). Type I IPNB is clinically similar to the familiar corresponding intraductal papillary mucinous neoplasm of the pancreas

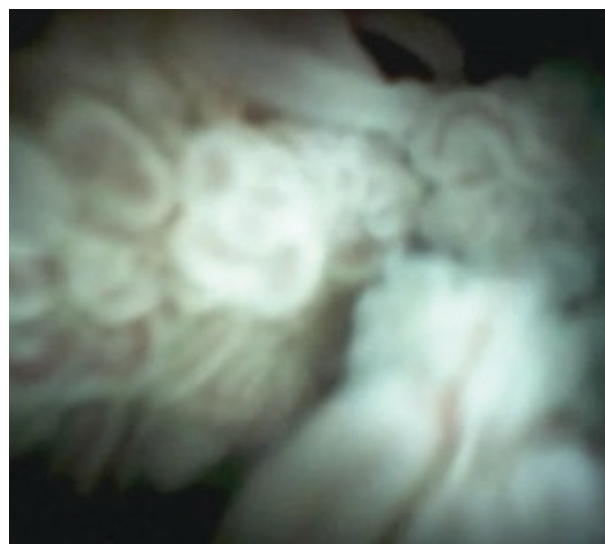


IMAGE COURTESY OF DANIEL STRAND, MD.

(IPMN). Type I IPNBs typically exhibit a superficial spreading growth pattern, copious mucin production, and progression through incremental dysplastic changes, eventually progressing to invasive biliary carcinoma. These lesions, described as both intrahepatic and extrahepatic tumors, comprise approximately 10% of resectable biliary tumors and were included in the 2010 World Health Organization Classification of Tumors of the Digestive System. Although this variant of bile duct cancer offers better overall survival than a traditional cholangiocarcinoma, lower median survival has been associated with tumor invasion depth, margin-positive resection, and lymph node metastasis. The only answer choice

that includes the potential for long-term, disease-free survival is surgical margin-free resection. As these lesions may be multicentric, particularly in cases of late recurrence (at >10 years), bile duct excision is warranted. All other forms of intervention including decompressive stent placement alone (Choice A), ERCP directed local therapies (Choice B), radiotherapy (Choice C), and chemotherapy (choice D) would be pursued with palliative intent.

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Question 8

A 43-year-old woman is seen in outpatient consultation for intermittent right upper quadrant pain. She reports experiencing bouts of severe, debilitating pain, which occur infrequently (one or twice monthly) for the preceding 9 months. Six months ago, she underwent elective laparoscopic cholecystectomy for these symptoms, which have continued unabated. After surgery, these symptoms prompted 3 additional emergency department visits, which failed to elucidate a diagnosis. Previous laboratory testing during episodes of pain have included normal liver biochemistries, complete

blood counts, and serum pancreatic enzymes. Additionally, 2 right upper quadrant ultrasounds have been unremarkable, and contrasted magnetic resonance imaging with cholangiopancreatography demonstrated a normal pancreatobiliary axis. Her symptoms are debilitating, and her referring physician asks you to address the question of a biliary sphincter disorder.

Which of the following interventions would you recommend?

- A. Diagnostic upper endoscopy (EGD)
- B. Endoscopic retrograde cholangiopancreatography (ERCP) with biliary sphincterotomy alone
- C. ERCP with pancreatic (Wirsung) and biliary sphincterotomy
- D. ERCP with pancreatic (Wirsung) sphincterotomy
- E. ERCP with sphincter of Oddi manometry

CORRECT ANSWER: A

RATIONALE

The patient presents with postcholecystectomy biliary-type pain. Although sphincter of Oddi disorders were historically classified by the Milwaukee subtypes of sphincter of Oddi dysfunction (SOD; types I, II, III), this system of classification is outdated and has been more appropriately supplanted by the Rome IV classification system of SOD. Papillary stenosis (formerly type I SOD) includes patients with overt and objective findings of biliary or pancreatic duct obstruction, whereas patients with some objective findings (either duct dilation or abnormal biochemistries) are best termed suspected functional biliary sphincter disorder (FBSO). The EPISOD (Evaluating Predictors & Interventions in Sphincter of Oddi Dysfunction) trial demonstrated that patients with type III SOD did not respond to sphincter ablation better than sham intervention. These patients are best classified as those with “functional biliary-type pain.” The diagnosis of a functional biliary pain disorder is one of exclusion, however, and diagnostic upper

endoscopy is indicated to assess for alternative (and common) organic causes of upper abdominal pain, such as peptic ulceration. As this patient does not meet diagnostic criteria for either organic papillary stenosis or FBS, performance of an ERCP is contraindicated due to procedural risk (most notably post-ERCP pancreatitis).

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Question 9

A 56-year-old man with familial adenomatous polyposis syndrome is seen for endoscopic resection of an ampullary adenoma. Prior assessment of his lesion demonstrated an 18-mm exophytic, nonulcerated-appearing polyp, which involves a shared pancreatobiliary orifice. Biopsies confirm a tubulovillous adenoma without evidence of dysplasia or local invasion. Preresection magnetic resonance imaging with cholangiopancreatography and endoscopic ultrasound reveal no evidence of invasion of the lesion beyond the duodenal mucosa or significant ductal extension. When discussing the risks of ampullectomy, the patient asks about the potential for pancreatitis after endoscopic retrograde cholangiopancreatography.

Which of the following maneuvers would you recommend for reducing this patient's overall risk of postprocedure pancreatitis?

- A. Complete endoscopic pancreatic sphincterotomy
- B. Piecemeal resection with subsequent ablation using argon plasma coagulation
- C. Pancreatic duct stent placement after resection
- D. Pancreatic duct stent placement before en bloc resection
- E. Resection using underwater mucosal resection technique

CORRECT ANSWER: C

RATIONALE

The overall risk of postprocedure pancreatitis (PEP) after endoscopic ampullectomy is significant, often cited as approaching 15% to 30%. Both nonrandomized and randomized data support the use of prophylactic pancreatic duct stents to reduce this risk significantly. A meta-analysis by Singh et al suggested a nearly 3-fold increased risk of PEP in patients who did not receive a pancreatic duct stent (15.5% vs 5.8%), with an estimated number needed to treat of 1 in every 10 patients. Pancreatic duct stent placement is typically performed after resection, as placement before en bloc resection would require transection of the stent during ampullectomy. Historically, conventional endoscopic mucosal resection (EMR) has been used for endoscopic ampullectomy, with or without a submucosal injection. Underwater mucosal resection (U-EMT) is a relatively new resection modality that has been employed successfully at the major papilla for resection. U-EMR employed in this way is limited to retrospective reports with little data to support an overall change in the incidence of PEP. Pancreatic sphincterotomy, although commonly performed after ampullectomy, is a risk factor for post-ERCP pancreatitis when employed without the addition of a pancreatic duct stent. Likewise, piecemeal resection and subsequent ablation around the pancreatic orifice (although safe with the addition of a pancreatic duct stent) has not been shown to decrease the incidence of PEP.

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Question 10

A 72-year-old man with atrial fibrillation, primary sclerosing cholangitis, and a left lobe intrahepatic cholangiocarcinoma is admitted to the hospital due to new-onset right upper quadrant pain, jaundice, and melena. Three days before admission he underwent a percutaneous liver

biopsy, which affirmatively diagnosed his malignancy. Vital signs obtained in the emergency department demonstrate a normal heart rate and blood pressure and no orthostatic hypotension. Laboratory tests show the following levels displayed below.

His INR is elevated in the context of concurrent warfarin use for atrial fibrillation.

What is the most appropriate next step in management?

- A. Computed tomography angiography and coagulopathy correction
- B. Diagnostic upper endoscopy
- C. Endoscopic retrograde cholangiopancreatography
- D. Left hepatic lobectomy
- E. Urgent percutaneous angiography and hepatic artery embolization

CORRECT ANSWER: A

RATIONALE

The patient presents with Quincke's triad of jaundice, right upper quadrant pain, and gastrointestinal bleeding, which is classically described in the setting of hemobilia. In addition, he has 2 risk factors for hemobilia including a biliary tract malignancy and recent instrumentation from percutaneous liver biopsy. Although blunt-force trauma was historically considered the leading cause of hemobilia, iatrogenic causes now account for more than two-thirds of reported cases. In specific, percutaneous interventions such as liver biopsy and transhepatic biliary drainage

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	234	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	152	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	175	10-40
Bilirubin (total), serum, mg/dL	4.2	0.3-1.0
Hemoglobin, blood, g/dL	7.6	14-18
International normalized ratio	5.2	<1.1
Leukocyte count, cells/ μ L	11,000	4000-11,000

are among the most common inciting factors.

Etiologies of hemobilia that are noniatrogenic may include malignancy, portal biliopathy, cholangitis (often parasitic), or protracted ductal obstruction. Most cases of hemobilia can be effectively managed (if necessary) by angiographic intervention, although supportive care alone is indicated in instances of minor bleeding. The current patient is hemodynamically stable, does not require immediate transfusion, and presents with a vitamin K antagonist-exacerbated coagulopathy. As such, supportive care (including correction of coagulopathy) and an image-guided assessment to find a meaningful vascular target are warranted as the next best step in management. Diagnostic upper endoscopy and endoscopic retrograde cholangiopancreatography (ERCP) may assist in diagnosis of hemobilia but may not be of therapeutic value for hemostasis. ERCP can be indicated in some cases, particularly for relief of concurrent acute cholangitis or malignancy-derived bleeding but is likely to be less helpful after liver biopsy. Left hepatic lobectomy is potentially useful for resection of the patient's neoplasm but is not indicated emergently in the hemodynamically stable patient. Urgent percutaneous angiography and hepatic artery embolization would be correct in the setting of hemodynamic instability but is less attractive given the patient's supratherapeutic INR.

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Question 11

A 38-year-old woman with a history of known gallstones presents in outpatient consultation for symptoms of occasional bloating, excessive flatus, and alternating constipation and diarrhea. During the detailed history, she informs you that she is a foster parent. On at least 3 separate occasions, children she has cared for have had an unusual illness of high fever, abdominal pain, headaches, and rose-colored spots on their chest. She also reports that outbreaks of similar symptoms have occurred among her coworkers after a potluck office party and after a neighborhood barbecue. What is the most appropriate next step in management?

- A. Antibiotic therapy
- B. Cholecystectomy
- C. Colonoscopy with mucosal biopsies
- D. Esophagogastroduodenoscopy with duodenal biopsies
- E. Typhoid conjugate vaccine

CORRECT ANSWER: B

RATIONALE

This patient's presentation is highly suggestive of an asymptomatic *Salmonella typhi* carrier state. The syndrome of illness experienced by patient contacts is consistent with the classic definition of typhoid fever. Chronic persistent carriage of *S typhi* can be potentiated by gallstones, whereby the organisms form a biofilm rendering antibiotic therapy ineffective at eradicating the colonization. Cholecystectomy is indicated, as it is the most effective means of eradicating the carrier state (although imperfect). Additionally, patients with asymptomatic *Salmonella* colonization are thought to have an increased risk of subsequently developing gallbladder carcinoma. Mucosal biopsy, either of the upper or lower gastrointestinal tract, are not effective means of establishing this diagnosis. Typhoid vaccination, which can be effective in the prevention of typhoid fever among unexposed patients, does not serve to eradicate the persistence of organisms within asymptomatic carrier(s).

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Question 12

A 32-year-old woman with a history of Roux-en-Y gastric bypass surgery and recent cholecystectomy is admitted to the hospital with acute right upper quadrant pain, nausea, and vomiting. Her vital signs are remarkable only for mild tachycardia, and laboratory testing shows the following levels displayed below.

A right upper quadrant ultrasound reveals a 12-mm diameter common bile duct and a 5-mm hyperechoic, shadowing focus in the lower third of the bile duct consistent with a bile duct stone. The intrahepatic ducts are nondilated. Gastroenterology consultation is requested to pursue endoscopic retrograde cholangiopancreatography (ERCP) in the setting of surgically-altered anatomy. When discussing various interventions with the patient, she is highly concerned with periprocedural risks.

Which of the following approaches to biliary intervention would you choose to lower overall risk of an adverse event in this patient?

- A. Balloon-enteroscopy assisted ERCP
- B. Endoscopic ultrasound (EUS)-directed

transluminal ERCP

- C. Laparoscopy-assisted ERCP with subsequent Stamm gastrostomy
- D. Laparotomy with common bile duct exploration
- E. Percutaneous transhepatic biliary drainage

CORRECT ANSWER: A

RATIONALE

Multiple endoscopic and nonendoscopic methodologies for biliary intervention in the setting of altered upper gastrointestinal anatomy have been described. Balloon-assisted ERCP has been observed to have the best overall safety profile with a statistically significantly lower rate of overall adverse events when compared with other biliary interventions in a recent meta-analysis. From the perspective of safety alone, this method offers advantages over both laparoscopy-assisted and EUS-directed transluminal ERCP. The major limitation of balloon-assisted ERCP is a consistently lower technical and clinical success than the alternative endoscopic approaches. Laparotomy and open bile duct exploration can be an effective intervention for retained common bile duct stone(s) and may be superior in terms of treatment in the setting of an in situ gallbladder. No comparative data exist in the absence of a gallbladder (as in this question), and open surgical intervention in this patient would be performed in the context of several prior abdominal operations. Percutaneous transhepatic biliary drainage can also be effective, particularly in setting of dilated intrahepatic ducts, although the incidence of reported bleeding adverse events may approach 15%.

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Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	178	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	245	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	205	10-40
Bilirubin (total), serum, mg/dL	2.4	0.3-1.0
Leukocyte count, cells/ μ L	10,000	4000-11,000

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Question 13

A 12-year-old woman is admitted to the hospital with right upper quadrant pain, jaundice, and pruritis. Her vital signs are unremarkable. Initial laboratory testing reveals the following results:

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	420	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	105	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	154	10-40
Bilirubin (total), serum, mg/dL	5.4	0.3-1.0
Carbohydrate antigen 19-9, serum, U/mL	650	0-37



IMAGE COURTESY OF DANIEL STRAND, MD.

A transabdominal ultrasound suggests biliary dilation, and a subsequent magnetic resonance cholangiopancreatography demonstrates the findings seen below. Her pancreatic duct anatomy is unremarkable, and contrasted sequences do not demonstrate a mass lesion. (see below left)

Which of the following would you recommend for definitive management?

- A. Choledochoduodenostomy
- B. Endoscopic retrograde cholangiopancreatography with sphincterotomy
- C. Extrahepatic biliary resection
- D. Ursodeoxycholic acid

CORRECT ANSWER: C

RATIONALE

The patient presents with obstructive jaundice due to a type Ic (vs IV) congenital biliary cyst by Todani classification. The clinical presentation of biliary cysts can include obstructive jaundice and/or pain (70%), cholangitis (22%), or pancreatitis (10%). Children are likely to present with obstruc-

tive symptoms, whereas adults are more likely to present with pain and/or cholangitis. Type I/IV congenital biliary cysts, such as the one shown above, are associated with an increased risk of biliary tract cancers (both gallbladder cancer and cholangiocarcinoma). This risk is particularly apparent in symptomatic patients who present at a younger age, although little data exist on asymptomatic patients discovered in adulthood. The exact risk of developing biliary neoplasia is not clear, but in symptomatic patients has been estimated to be between 10% and 30%. Surgical resection of the extrahepatic biliary tree is the appropriate destination treatment for symptomatic

patients to mitigate the risk of neoplasia. The bile duct resection along with a hepatojejunostomy, which can be referred to as a pancreatoduodenectomy (Whipple operation). ERCP or drainage operations, although attractive for relief of obstruction, have not been shown to reduce the subsequent risk of cancer in long-term cohort studies. The remaining answer choices do not address the overall increased risk of neoplasm due to retained biliary epithelium.

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Question 14

A 32-year-old woman is evaluated in the outpatient clinic for recurrent acute pancreatitis. She has had at least 3 episodes of upper abdominal pain, nausea, and emesis with concurrent hyperamylasemia diagnostic for pancreatitis over the last 18 months. She does not drink alcohol, takes no prescription medications, and uses nonste-

roidal antiinflammatory drugs sparingly. Two right upper quadrant ultrasound examinations revealed no biliary lithiasis or significant extrahepatic duct dilation. After clinical consultation, you recommend a serum lipid panel and magnetic resonance imaging (MRI) of the abdomen with MR cholangiopancreatography to help identify a potential etiology. Her serum triglyceride level is 112 mg/dL (reference range, <50 mg/dL), and the results of her MRI are shown below.

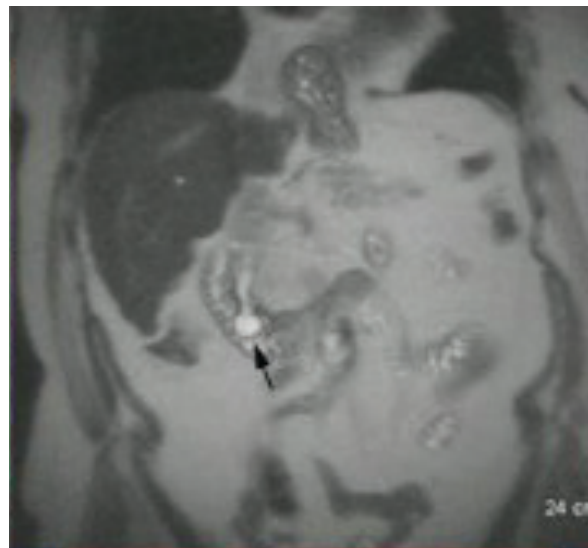


IMAGE COURTESY OF DANIEL STRAND, MD.

What is the most appropriate step in management to prevent recurrent pancreatitis?

- A. Choledochoduodenostomy
- B. Endoscopic retrograde cholangiopancreatography with sphincterotomy
- C. Extrahepatic biliary resection
- D. Fenofibrate treatment
- E. Pancreatoduodenectomy (Whipple operation)

CORRECT ANSWER: B

RATIONALE

The patient presents with obstructive jaundice due to a type III congenital biliary cyst by Todani classification. Unlike other congenital cysts, these are limited to the intraduodenal portion of the common bile duct and are typically lined by bland duodenal or biliary epithelium. Additionally, they have little to no neoplastic risk and therefore do not typically require surgical management. Endoscopic retrograde cholangiopancreatography with complete biliary sphincterotomy (or snare cyst-papillectomy) can offer definitive management. Unlike other biliary cysts, patients with type III (choledochocoele) congenital cysts present much more commonly with pancreatitis (40%-70%) than with other complications (obstructive jaundice, among others). Treatment with fenofibrate, although important in the management of

hypertriglyceridemia-induced pancreatitis, has little benefit in this clinical scenario.

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Question 15

A 35-year-old man with type 1 diabetes mellitus from rural Appalachia is admitted to the hospital for progressively abnormal liver biochemistry levels, which were first noted 4 weeks ago when he was seen by his primary care physician for symptoms of nausea, diarrhea, and vague abdominal pain. On presentation to the emergency department, he endorses the interval development of fever, chills, and right upper quadrant pain. Laboratory tests reveal the following shown below.

Laboratory Test	Result 4 weeks ago	Result Today	Reference Range
Alkaline phosphatase, serum, U/L	460	980	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	156	499	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	122	334	10-40
Bilirubin, total, serum, mg/dL	1.4	7.9	0.3-1.0

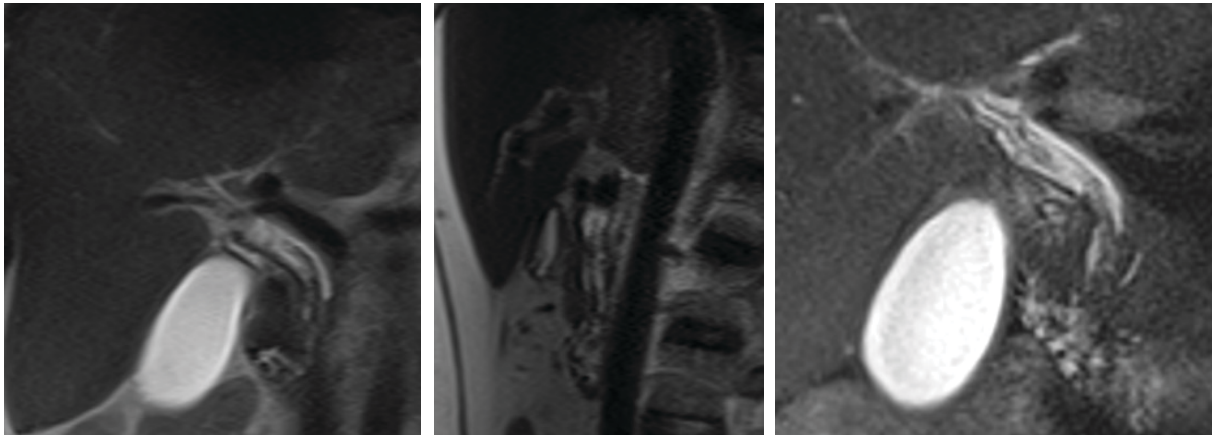


IMAGE COURTESY OF DANIEL STRAND, MD.

A computed tomography scan performed 3 weeks ago demonstrated new-onset dilation of the extrahepatic biliary tree (not shown), and a subsequent magnetic resonance cholangiopancreatography at the time of hospital admission is also shown with the laboratory results.

Which of the following statements is most accurate about the diagnosis of this patient's disease?

- A. Serologies are an effective way to diagnose this entity
- B. Symptoms will subside once the organisms die
- C. Organisms remain in bile ducts and do not extend into the pancreatic duct
- D. Pulmonary involvement results in high fevers and toxic presentation
- E. Stool microscopy is used for ova identification

CORRECT ANSWER: E

RATIONALE

The patient presents with classic features of biliary and intestinal ascariasis. In specific, this case vignette is compatible with the retention of dead ascaris within the biliary tree, owing to the duration (>3 weeks) and concurrent presence of likely pyogenic cholangitis.

Although uncommon in the United States, ascariasis infects approximately 25% of the world's population and is particularly common in Southeast Asia and the Indian subcontinent. In the United States, ascariasis is more common in the Southeast (particularly Appalachia) and among small, independent pig farmers.

Biliary infection accounts for 10% to 20% of hospitalizations due to ascariasis. Anthelmintic agents such as albendazole, mebendazole, and ivermectin are associated with high parasitological cure rates and large reductions in the number of eggs present in feces. This is the most common

modality of diagnosis for this disease process. Stool examination and identification of ova/eggs will usually be present 40 days after the onset of pulmonary symptoms.

Although live organisms in the biliary tree typically cause colic, pyogenic infections (including cholangitis and liver abscess) are much more commonly seen with dead ascaris carcasses than with live worms. Organisms can extend from the bile duct into the pancreatic duct and cause acute pancreatitis. Serologies are not an effective mode of diagnosis in this disease process and is reserved for epidemiologic studies. IgG antibodies which appear do not seem to have protective properties.

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Conterno LO, Turchi MD, Corrêa I, Monteiro de Barros Almeida RA. Anthelmintic drugs for treating ascariasis. *Cochrane Database Syst Rev*. 2020;4(4):CD010599. Published 2020 Apr 14. doi:10.1002/14651858.CD010599.pub2

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Question 16

A 72-year-old woman is seen in the emergency department with acute-onset right upper quadrant abdominal pain. Upon evaluation, she is noted to have a heart rate of 105 bpm and a temperature of 38.3 °C.

Laboratory tests reveal the results shown at the top on the following page.

Right upper quadrant ultrasound reveals a 14-mm diameter common bile duct, cholelithiasis without

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	225	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	475	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	430	10-40
Bilirubin (total), serum, mg/dL	4.2	0.3-1.0
International normalized ratio	1.0	<1.1
Leukocyte count, cells/ μ L	18,000	4000-11,000
Lipase, serum, U/L	35	10-140
Platelet count, plts/ μ L	160,000	150,000-450,000

gallbladder wall thickening, and no pericholecystic fluid. The patient is administered intravenous Ringers' lactate, admitted to the hospital, and started on parenteral antibiotics.

What is the most appropriate next step in management?

- A. Cholecystectomy
- B. Endoscopic retrograde cholangiopancreatography with duct clearance and stent placement
- C. Endoscopic retrograde cholangiopancreatography with stent placement
- D. Magnetic resonance cholangiopancreatography
- E. Percutaneous transhepatic biliary drainage

CORRECT ANSWER: B

RATIONALE

The patient presents with Charcot's triad of fever, jaundice, and abdominal pain, which is consistent with a diagnosis of acute cholangitis. The appropriate management of suppurative infections of the biliary tree includes supportive care, systemic antibiotics, and source control via biliary decompression. Endoscopic retrograde cholangiopancreatography (ERCP) is the preferred method of biliary decompression in most patients with conventional upper gastrointestinal anatomy due to high clinical success rate, relatively short length of hospitalization, and lower risk of adverse events than alternatives. The rationale to perform decompression alone (versus duct clearance) is based upon observational data, which suggest an increased risk of bleeding in patients with cholangitis who undergo biliary sphincterotomy. Perform-

ing concurrent ductal clearance is associated with more rapid clinical and biochemical improvement (normalization of leukocyte count, liver enzymes), shorter hospital length of stay, and need for fewer subsequent ERCP procedures. Although some circumstances warrant biliary decompression alone (coagulopathy, physiological compromise from cholangitis, ongoing antithrombotic use), combined endotherapy and decompression is favored in patients who are not critically ill, and this strategy is reflected in current guidelines. In the setting of acute cholangitis, further imaging with magnetic resonance cholangiopancreatography is not indicated. Cholecystectomy may eventually be needed, but with bile duct dilatation, the ERCP is more pressing. Finally, ERCP would lead to less morbidity than transhepatic biliary drainage where a percutaneous tube would be left behind.

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Question 17

A 19-year-old man with a history of hereditary spherocytosis is admitted to the hospital with

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	200	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	140	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	180	10-40
Bilirubin, serum		
Total, mg/dL	2.4	0.3-1.0
Direct, mg/dL	1.9	0.1-0.3
Hemoglobin, blood, g/dL	9.2	14-18
Lactate dehydrogenase, serum, U/L	280	80-225
Platelet count, <i>plts</i> /μL	160,000	150,000-450,000
Reticulocyte count, % of red cells	10	0.5-1.5

acute-onset right upper quadrant pain and nausea for 4 hours. He has had several prior episodes of similar symptoms, which spontaneously improved and required no medical attention. Typically, episodes have occurred after a meal, although not exclusively. In the emergency department he is afebrile, normotensive, and has a heart rate of 110 bpm. His physical examination demonstrates a thin male in mild distress, with right upper quadrant abdominal tenderness without rebound, rigidity, or inspiratory arrest on palpation. He has palpable splenomegaly. Laboratory tests show the following levels displayed above.

Right upper quadrant ultrasound reveals a 10-mm diameter common bile duct, in situ gallbladder, and cholelithiasis. The intrahepatic biliary tree is nondilated.

The patient is most likely to have which of the following?

- A. Black pigment stones
- B. Brown pigment stones
- C. Cholesterol stones
- D. Cirrhosis
- E. Recurrent pyogenic cholangitis

CORRECT ANSWER: A

RATIONALE

The patient presents with signs and symptoms of typical biliary colic. His clinical history, physical examination, and laboratory testing is consistent with hereditary spherocytosis (HS), which is a dis-

order of erythrocyte membrane structure caused by several known genetic mutations. As a syndrome, HS is characterized by splenomegaly, hemolytic anemia, gallstones, and hypercoagulability. Black pigmented gallstones are commonly associated with chronic hemolytic states and represent the majority of noncholesterol stones identified in western countries. Brown pigment stones are associated with recurrent pyogenic cholangitis, which is uncommon in the United States and associated with possible parasitic infection(s) in endemic areas, such as Southeast Asia, although causality is unclear. Recurrent pyogenic cholangitis typically results in ectatic intrahepatic ducts with adjacent structuring, which is not apparent in this case. The patient presented here does not have stigmata of end-stage liver disease to suggest a diagnosis of cirrhosis, and the palpable splenomegaly is a physical finding of splenic sequestration, rather than an identifying feature of portal hypertension.

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Trotman BW. Pigment gallstone disease. *Gastroenterol Clin North Am*. 1991;20(1):111-126.

Question 18

A 26-year-old woman with no past medical history is seen in outpatient consultation to discuss incidental findings on recent cross-sectional imaging. She was previously evaluated at her local emer-

gency department after sustaining minor injuries during a motor vehicle crash and had undergone computed tomography of the abdomen, which suggested anatomical variation of her pancreatobiliary axis. Contrast-enhanced magnetic resonance imaging with cholangiopancreatography was ordered by her primary care physician in anticipation of specialty consultation. This study revealed a 2-cm shared channel between the ventral pancreatic duct and common bile duct, which join at a right angle outside the duodenal wall. The extrahepatic biliary tree is 6 mm in diameter, and the pancreatic duct is normal in size. There is no pancreas divisum. Liver biochemistry and serum amylase levels are unremarkable. Which of the following management strategies is most appropriate in this patient?

- A. Cholecystectomy
- B. Endoscopic retrograde cholangiopancreatography with sphincterotomy
- C. Close observation
- D. Surgical choledochoduodenostomy
- E. Ursodeoxycholic acid

CORRECT ANSWER: A

RATIONALE

The patient presents with a Komi type I anomalous pancreatobiliary junction (APBJ). She is asymptomatic and the biliary tree is nondilated, suggesting the absence of a concurrent congenital biliary cyst. APBJ carries an overall increased risk of carcinogenesis within the biliary tract, and the risk of gallbladder carcinoma is most significant for patients without bile duct dilation. This risk has been estimated to be up to 40% in long-term observational studies. Elective, prophylactic cholecystectomy is appropriate in all patients with APBJ for this reason. Although ERCP with sphincterotomy may be useful in some patients with amenable anatomy, the ductal confluence of the patient described above cannot be separated in this fashion. Although the patient is asymptomatic, close observation is inappropriate because it fails to address the considerable morbidity and mortality from gallbladder cancer in this patient population. Drainage operations

for diversion do not seem to appreciably alter the risk of subsequent biliary tract cancer and would generally be considered inappropriate without a dilated bile duct. Likewise, ursodeoxycholic acid, although potentially useful in the setting of biliary lithiasis, does not alter the risk of carcinogenesis due to pancreatic juice reflux.

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Question 19

A 62-year-old woman with alcohol-related cirrhosis is admitted to the hospital with progressive jaundice. A right upper quadrant ultrasound demonstrates perihepatic ascites and hepatofugal Doppler flow in the portal vein with numerous collaterals. Endosonography reveals the following finding, which is associated with biliary obstruction.



IMAGE COURTESY OF DANIEL STRAND, MD.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	1200	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	52	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	82	10-40
Bilirubin (total), serum, mg/dL	12	0.3-1.0
Creatinine, serum, mg/dL	1.2	0.7-1.5
International normalized ratio	1.8	<1.1
Platelet count, <i>plts</i> /μL	45,000	150,000-450,000
Platelet count, <i>plts</i> /μL	160,000	150,000-450,000

On presentation, she is icteric and overtly jaundiced but is without confusion or fever. Laboratory results are above.

For definitive management you would recommend which of the following?

- A. Endoscopic retrograde cholangiopancreatography with biliary sphincterotomy
- B. Endoscopic retrograde cholangiopancreatography with plastic stent placement
- C. Percutaneous transhepatic biliary drainage
- D. Transjugular intrahepatic portosystemic shunt
- E. Ursodeoxycholic acid

CORRECT ANSWER: D

RATIONALE

The patient presents with features of portal biliopathy in the setting of known portal hypertension secondary to alcohol-related cirrhosis. Portal biliopathy is characterized by extrinsic compression of the biliary tree from engorged paracholedochal, epicholedochal, or cholecystic veins. This clinical entity most commonly results in cholestasis from biliary obstruction but may also present with hemobilia or biliary calculi. Portal biliopathy is most commonly the result of portal vein thrombosis or cavernous transformation but may also occur as a result of portal hypertension from intrinsic liver disease. Definitive relief of obstruction from portal biliopathy can be provided by biliary bypass or creation of a portosystemic shunt. In cases where cavernous transformation or portal vein thrombosis is the underlying etiology, the extent of vascular thrombosis may preclude this intervention.

Endoscopic retrograde cholangiopancreatography (ERCP) with biliary sphincterotomy alone is insufficient as initial management. ERCP with plastic stent placement is commonly employed for immediate relief of obstruction in portal biliopathy but does not provide definitive management. Percutaneous transhepatic biliary drainage can be a reasonable alternative in some cases for immediate relief of obstruction but should generally be avoided in the presence of ascites. Ursodeoxycholic acid, although potentially helpful as an adjunct agent, also does not provide definitive intervention for biliary obstruction.

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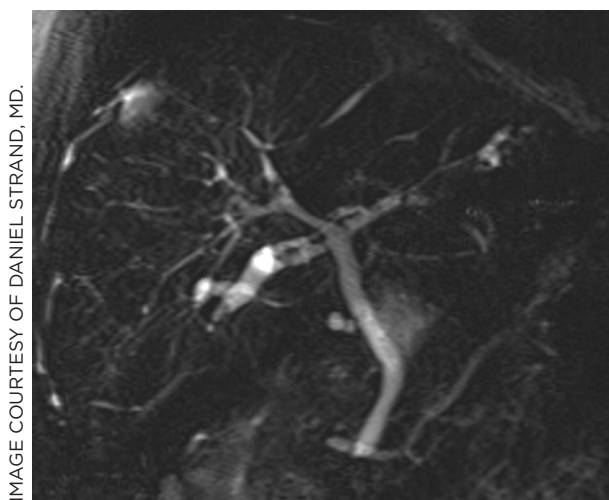
Question 20

A 48-year-old man is evaluated in the clinic for abnormal liver biochemistry levels. He is referred to you after his primary care physician noted

Laboratory Test	Result 6 months ago	Result Current	Reference Range
Alkaline phosphatase, serum, U/L	370	440	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	58	65	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	65	78	10-40
Bilirubin, total, serum, mg/dL	1.5	1.3	0.3-1.0

persistently elevated enzymes for 9 months, which had formerly been unremarkable. On interview, he reports symptoms of mild pruritis, irregular bowel movements, and diminished energy but is otherwise without complaints. His vital signs are normal, and his physical examination is unremarkable. His liver biochemistry levels (6 months ago and currently) are reported above.

Magnetic resonance (MR) imaging of the abdomen is performed and shows no mass lesion on contrasted image sequences. The MR cholangiogram is demonstrated a below.



What is the next best step in management?

- A. Antimitochondrial antibody titers
- B. Colonoscopy
- C. Endoscopic retrograde cholangiopancreatography with biliary sphincterotomy
- D. Transjugular liver biopsy
- E. Ursodeoxycholic acid 28 to 30 mg/kg daily

CORRECT ANSWER: B

RATIONALE

This asymptomatic patient presents with classic primary sclerosing cholangitis (PSC), which is diagnosed definitively by the characteristic MR cholangiogram seen above. At diagnosis, most patients (up to 80%) with PSC have concurrent inflammatory bowel disease, which is most commonly ulcerative colitis. This association is especially true for male patients, who have an approximate 2- to 3-fold increased incidence when compared with female patients with PSC. Given the high degree of concurrent disease, and an observed increased risk of colorectal cancer in these patients, colonoscopy is indicated at the time of diagnosis. Antimitochondrial antibody titers and ursodeoxycholic acid are useful in the diagnosis and management of primary biliary cholangitis (PBC), which is a mimicker of small-duct PSC and has demographic female predominance. Additionally, toxicity may occur in patients treated with high-dose (28-30 mg/kg daily) ursodeoxycholic acid. Endoscopic retrograde cholangiopancreatography (ERCP) can be invaluable in select patients with PSC to evaluate for concurrent neoplasia, relieve a dominant stricture, or treat pyogenic cholangitis. In this case, a definitive indication for ERCP is not present, and biliary sphincterotomy may actually increase the long-term risk of bacterial cholangitis. Transjugular liver biopsy may be useful in the case of a diagnostic uncertainty or when assessing overlap with autoimmune hepatitis, but the patient's cholangiogram is sufficient to diagnosis large-duct PSC in this example.

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Chapman R, Fevery J, Kalloo A, et al. Diagnosis and management of primary sclerosing cholangitis. *Hepatology*. 2010;51(2):660-678. doi:10.1002/hep.23294

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	860	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	143	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	158	10-40
Bilirubin, total, serum, mg/dL	4.3	0.3-1.0

Chapman MH, Thorburn D, Hirschfield GM, et al. British Society of Gastroenterology and UK-PSC guidelines for the diagnosis and management of primary sclerosing cholangitis. *Gut*. 2019;68(8):1356-1378. doi:10.1136/gutjnl-2018-317993

Question 21

A 57-year-old man is being followed up longitudinally in the clinic for large-duct primary sclerosing cholangitis (PSC). Although asymptomatic for many years, he has recently experienced the insidious development of pruritis and scleral icterus, which his spouse noted earlier this week.

After consultation, he is sent for a set of liver biochemistry tests; results are reported above.

Magnetic resonance imaging of the abdomen is performed. Although no discrete mass is seen, a new dominant stricture is noted at the hepatic confluence, involving the common hepatic duct and right hepatic duct. In addition, he has had interval development of splenomegaly suggestive of concomitant cirrhosis.

Which of the following is the next best step in the management of this patient?

- A. Focal liver biopsy of the hilum
- B. Corticosteroids
- C. Nonfocal liver biopsy
- D. Endoscopic retrograde cholangiopancreatography with biliary brush cytology
- E. Prophylactic antibiotics

CORRECT ANSWER: D

RATIONALE

The patient presents with progressive cholestasis due to a dominant stricture in the setting of PSC. Corticosteroids and other immunosuppressive drugs have been studied as treatment of classic PSC due to its close association with inflammatory bowel disease and the widespread use of these agents in that disease. Neither observational data nor small randomized trials have supported the use of steroids for improvement in PSC disease activity or other clinical outcome(s). Current available guidelines argue against the use of these agents for treatment of PSC; therefore, corticosteroids would be contraindicated in this patient. Focal biopsy of the hilum or non-focal biopsy of the liver would not be diagnostic or therapeutic for the biliary stricture. Endoscopic retrograde cholangiopancreatography (ERCP) is indicated in patients with PSC with a dominant stricture and cholestasis, both for diagnosis of neoplasia and intervention. Tissue sampling, which can include either cholangioscopic biopsy or brush cytology is indicated (with or without fluorescent in situ hybridization) to detect neoplasia. Although some strictures in PSC may require stent placement, many will respond to balloon dilation alone, which is acceptable when technically feasible due to its low complication rate. Prophylactic antibiotics are indicated at the time of ERCP due to high rates of observed cholangitis in patients who undergo instrumentation procedures without prophylaxis (up to 36%), but not as the singular treatment.

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Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	690	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	110	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	104	10-40
Bilirubin (total), serum, mg/dL	2.4	0.3-1.0

Hirota WK, Petersen K, Baron TH, et al. Guidelines for antibiotic prophylaxis for GI endoscopy. *Gastrointest Endosc.* 2003;58(4):475-482. doi:10.1067/s0016-5107(03)01883-2

Question 22

A 29-year-old man from West Africa is admitted to the hospital due to abdominal pain, low-grade fever, and diarrhea. He reports intermittent bouts of right upper quadrant pain, radiating to his right shoulder, and accompanied by persistent loose, nonbloody stools. Physical examination demonstrates temporal atrophy, mild tenderness in the right upper quadrant, and abdominal tympani.

Laboratory testing demonstrates the following liver biochemistry levels shown above.

A right upper quadrant ultrasound reveals dilation of the intra- and extrahepatic ducts without visible stone but an obscured distal common bile duct due to overlying bowel gas. Magnetic resonance imaging with cholangiopancreatography demonstrates a short, distal bile duct stricture with upstream dilation, and several intrahepatic ducts giving a beaded appearance. No mass lesion is seen at the ampulla, pancreas, or bile duct.

Which of the following laboratory results would support the most likely diagnosis?

- A. CD4 T cell count of 50 cells/ μ L
- B. Elevated carbohydrate antigen 19-9
- C. IgG4 level of 14 mg/dL
- D. Positive antimitochondrial antibody
- E. Positive anti-smooth muscle antibody

CORRECT ANSWER: A

RATIONALE

The patient presents with biliary obstruction secondary to papillary stenosis and irregular intrahepatic ducts, which suggest concurrent intrahepatic sclerosing cholangitis. This constellation of cholangiographic features is the most common variant of HIV cholangiopathy, although this disease can present with either sclerosing cholangitis or papillary stenosis alone. The clinical history of abdominal pain, diarrhea, and low-grade fever is also typical. Approximately 80% of cases of HIV cholangiopathy are associated with low CD4 T cell counts, usually less than 100 cells/ μ L. Elevated carbohydrate antigen 19-9, which is typically associated with pancreatobiliary malignancy, may be nonspecific at low-level elevation, and a mass is not seen on cross-sectional imaging. Cholangiopathy from IgG4-related disease is an important differential diagnosis, but a low serum IgG4 level would not support his diagnosis.

The patient's sex and cholangiography findings do not suggest a diagnosis of PBC or autoimmune hepatitis (AIH), although smooth muscle autoantibodies can be seen in AIH/PSC overlap syndrome, which is more common in pediatric patients.

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Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.4	3.5–5.5
Alkaline phosphatase, serum, U/L	1270	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	110	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	134	10–40
Bilirubin (total), serum, mg/dL	5.4	0.3–1.0
International normalized ratio	1.1	<1.1

Question 23

A 57-year-old man is admitted to the hospital 6 months after orthotopic liver transplantation for Wilson's disease. His immediate postoperative course was uncomplicated, and routine monitoring, including protocol-based liver biopsies, has been unremarkable. On presentation, he reports a 1-month history of vague upper abdominal discomfort and intermittent low-grade fevers. Over the last week he has noted the insidious onset of generalized itching and scleral icterus. Physical examination demonstrates jaundice but no evidence of ascites, asterixis, or abdominal tenderness. Laboratory testing demonstrates the following results shown above.

After multidisciplinary discussion, an endoscopic retrograde cholangiopancreatography (ERCP) is performed, which reveals the following cholangiogram:



IMAGE COURTESY OF DANIEL STRAND, MD.

After completion of the ERCP, what is the most appropriate next step in management?

- A. Emergent retransplantation
- B. Right upper quadrant ultrasound with Doppler flow
- C. Serum antimitochondrial antibodies
- D. Thymoglobulin therapy
- E. Transcutaneous Liver biopsy

CORRECT ANSWER: B

RATIONALE

The patient presents with progressive cholestasis in the setting of multifocal, nonanastomotic biliary strictures. Strictures such as those seen above can be due to immunologic or inflammatory causes (primary sclerosing cholangitis, IgG4-related disease, etc) but may also be the result of ischemic injury (hepatic artery thrombosis, sclerosis, or transarterial chemoembolization).

Hepatic artery thrombosis (HAT) is a major cause of graft loss and transplant related mortality, comprising 60% of all hepatic transplant vascular complications. HAT may be classified as early (typically within 4 weeks) HAT or late HAT, which have differing clinical presentations. Early HAT is often characterized as acute, fulminant hepatic failure, whereas late HAT may present with insidious, progressive cholestasis. This latter course may present with (or without) symptoms of cholangitis or a liver abscess. The median time to diagnosis of HAT is appreciated to be about 6 months (1.8 to 79 months) after liver transplantation. Hepatic artery doppler ultrasound is useful in the diagnosis of early HAT but may be less sensitive for delayed thromboses due to the formation of multiple collaterals. An alternative for diagnosis, would be computed

Laboratory Test	Result 2 weeks ago	Result Today	Reference Range
Alkaline phosphatase, serum, U/L	780	350	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	175	36	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	234	45	10-40
Bilirubin, total, serum, mg/dL	3.6	0.9	0.3-1.0

tomography or magnetic resonance angiography. Emergent retransplantation is frequently required for early HAT in patients who present with fulminant hepatic failure. Late-onset HAT may be managed conservatively, though outcomes are still guarded. Graft function loss in late-onset HAT is often indolent, with long-term survival observed in only 33% of patients without the need for a second liver transplantation. Retransplantation without a work up to establish a diagnosis would be inappropriate. Serum antimitochondrial antibodies are a useful diagnostic test for primary biliary cholangitis, a diagnosis which is not supported by the vignette or the cholangiography findings. Thymoglobulin is potentially useful for treatment of rejection, but this is not established by the data presented. Liver biopsy can be helpful in identifying rejection, but findings in late-onset HAT with biliary ischemia may be nonspecific.

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Haque M, Schumacher PA, Harris A, et al. Late acute celiac and hepatic artery thrombosis with portal vein thrombosis resulting in hepatic infarction 12 years post orthotopic liver transplantation. *Ann Hepatol*. 2009;8(4):396-399.

Question 24

A 32-year-old man from Southeast Asia is seen in consultation after a recent emergency department visit. He presented 2 weeks ago to his local hos-

pital with acute-onset right upper quadrant pain, low-grade fever, and chills. During that visit, laboratory testing was performed, and he was given intravenous fluids and parenteral antibiotics and was ultimately discharged without admission. He was then given a prescription for a 10-day course of oral antibiotics, which he recently completed. He feels significantly better but has had at least 6 similar episodes over the past several years, beginning in his native country before immigrating to the United States.

His liver enzyme levels over time are presented as shown above. He brings a copy of a recent computed tomography scan for review, which shows the following finding:

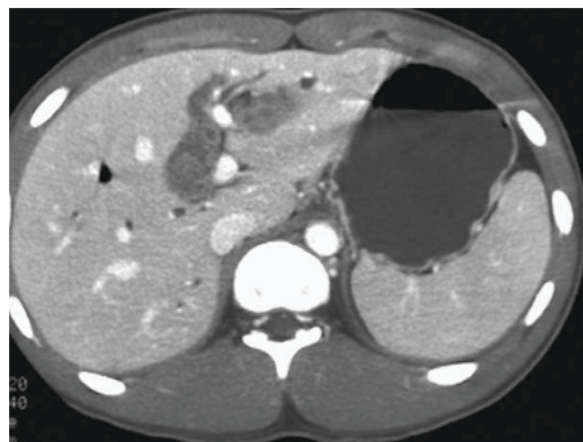


IMAGE COURTESY OF DANIEL STRAND, MD.

Which of the following is the most likely diagnosis?

- A. Black pigment stones due to hemolytic anemia
- B. Perihilar cholangiocarcinoma
- C. Primary sclerosing cholangitis
- D. Recurrent pyogenic cholangitis
- E. Systemic IgG4-related disease

CORRECT ANSWER: D

RATIONALE

The patient vignette is most consistent with a diagnosis of recurrent pyogenic cholangitis (RPC). This clinical syndrome is defined by the development of primary intrahepatic stones and recurrent acute cholangitis, most often in patients of East or Southeast Asian descent. Although historically associated with parasitic infections, including *Clonorchis sinensis* and *Ascaris lumbricoides*, the etiologic relationship between biliary parasitosis and RPC is unclear. *Ascaris* infects up to 25% of the global population, and RPC is seen primarily in Southeast Asia, suggesting a more complex pathophysiology. For unclear reasons, RPC tends to present with ectasia, dilation, and stone accumulation preferentially in the left biliary system.

Stones in RPC are typically brown pigment stones, rather than the black pigment stones seen in disorders of hemolysis. RPC and/or *Clonorchis spp.* infections are associated with an increased incidence of cholangiocarcinoma, although the patient presented in the vignette is relatively young (most cholangiocarcinomas present in the sixth decade of life) and does not have typical symptoms of a progressive neoplasia (weight loss, persistent cholestasis, etc). Primary sclerosing cholangitis typically presents with multifocal stricture(s) and not a stone-filled, dilated left biliary system as seen in this patient. Systemic IgG4-related disease can be a mimicker of sclerosing cholangitis or may present with extrahepatic biliary stricture(s). Although this disease may be considered in the differential, it is not likely, given the vignette provided.

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Tsui WM, Chan YK, Wong CT, Lo YF, Yeung YW, Lee YW. Hepatolithiasis and the syndrome of recurrent pyogenic cholangitis: clinical, radiologic, and pathologic features. *Semin Liver Dis*. 2011;31(1):33-48. doi:10.1055/s-0031-1272833

Question 25

A 25-year-old woman patient with recurrent pyogenic cholangitis presents to the clinic to discuss management of his disease. Over the past several years she has had at least 3 hospital admissions for acute abdominal pain, fever, and cholestasis. On each occasion she has responded effectively to parenteral antibiotics, although she did require endoscopic retrograde cholangiopancreatography (ERCP) with stent placement once to provide drainage. Magnetic resonance imaging performed in anticipation of this consultation, demonstrates no visible mass or extrahepatic biliary stricture.

Her disease is limited to the left biliary system, which is dilated and contains numerous stones. A stricture is present at the origin of the left hepatic duct; accordingly, the hepatic parenchyma appears atrophic.

Her liver enzyme levels are presented below.

Which of the following interventions is most appropriate to prevent long-term morbidity?

- A. ERCP with cholangioscopy directed lithotripsy and stent placement
- B. Left hepatectomy
- C. Left hepatectomy, bile duct resection, and hepatojejunostomy
- D. Percutaneous transhepatic drain placement and lithotripsy
- E. Ursodeoxycholic acid therapy

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	470	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	73	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	54	10-40
Bilirubin, total, serum, mg/dL	1.3	0.3-1.0

CORRECT ANSWER: B

RATIONALE

Recurrent pyogenic cholangitis (RPC) is a clinical syndrome characterized by the accumulation of intrahepatic brown pigment stones and repetitive bouts of acute cholangitis. Hepatic resection is associated with significantly fewer biliary strictures and recurrent cholangitis episodes in long-term follow up compared with minimally invasive approaches. Resection is especially favored in lobe-limited disease, when atrophy is present, or when cholangiocarcinoma is suspected (estimated incidence of up to 23%). ERCP and parenteral antibiotics can be highly effective for control of acute cholangitis, but long-term control of RPC by ERCP is not always feasible. Although hepatojejunostomy and bile duct excision may be necessary to manage recurrent cholestasis in patients with extrahepatic involvement, this is not the case in this patient. Compared with surgery, endoscopic and percutaneous approaches have lower rates of successful stone clearance and increased rates of cholangitis, liver abscess, or stone related complications. Ursodeoxycholic acid, although commonly used for primary sclerosing cholangitis (PBC), does not have a defined role in patients with RPC.

REFERENCES

Buxbaum JL, Lane CJ, Bagatelos KC, Ostroff JW. Long-term endoscopic management for primary recurrent pyogenic cholangitis. *J Dig Endosc.* 2014;5:64–68.

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gitis: Got Stones?. *Dig Dis Sci.* 2016;61(11):3147-3150. doi:10.1007/s10620-015-3973-5

Koh YX, Chiow AK, Chok AY, Lee LS, Tan SS, Ibrahim S. Recurrent pyogenic cholangitis: disease characteristics and patterns of recurrence. *ISRN Surg.* 2013;2013:536081. Published 2013 May 25. doi:10.1155/2013/536081

Tsui WM, Chan YK, Wong CT, Lo YF, Yeung YW, Lee YW. Hepatolithiasis and the syndrome of recurrent pyogenic cholangitis: clinical, radiologic, and pathologic features. *Semin Liver Dis.* 2011;31(1):33-48. doi:10.1055/s-0031-1272833

Question 26

A 55-year-old woman presents with lightheadedness, increasing right upper quadrant (RUQ) pain, and melena 12 hours after percutaneous liver biopsy was performed to evaluate abnormal liver serologies. On physical examination blood pressure is 85/55 mmHg sitting and 105/60 mmHg supine. Heart rate is 98 bpm. Abdominal examination is significant for RUQ tenderness to palpation. After receiving 1 L of fluid resuscitation intravenously, her blood pressure is 85/52 mmHg sitting and 105/65 mm Hg supine with heart rate of 108 bpm.

Laboratory results are shown below.

Which of the following investigations should be performed next?

- A. Angiography

Laboratory Test	Result 1 week ago	Result Today	Reference Range
Alkaline phosphatase, serum, U/L	115	210	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	98	120	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	55	85	10-40
Bilirubin, total, serum, mg/dL	0.8	1.4	0.3-1.0
Hemoglobin, blood, g/dL	12	9.8	12-16
Leukocyte (WBC) count, cells/ μ L	10,000	14,000	4000-11,000
Platelet count, plts/ μ L	155,000	140,000	150,000-450,000

- B. Endoscopic retrograde cholangiopancreatography
- C. Right upper quadrant ultrasound
- D. Tagged red blood cell scan
- E. Upper endoscopy

CORRECT ANSWER: A

RATIONALE

This patient has evidence of gastrointestinal bleeding after percutaneous liver biopsy. The most likely cause is hemobilia, resulting from injury to liver vasculature. Angiography (arteriography) to demonstrate the hepatic artery and its branches is the most direct way to confirm hemobilia due to arterial injury from liver biopsy. If the local anatomy is favorable, therapeutic embolization of the offending vessel can stop the bleeding. Endoscopic retrograde cholangiopancreatography has no role in the management of hemobilia. If the diagnosis is in doubt, direct inspection of the duodenal papilla using a side-viewing endoscope (duodenoscope) can be helpful. Standard upper endoscopy using an end-viewing instrument may fail to visualize the duodenal papilla. Ultrasound and computed tomography scanning are typically unhelpful in this situation. Tagged red blood cell scans are used as the standard for active lower GI bleeding.

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- Moodley J, Singh B, Lalloo S, Pershad S, Robbs JV. Non-operative management of haemobilia. *Br J Surg*. 2001;88(8):1073-1076. doi:10.1046/j.0007-1323.2001.01825.x

Question 27

A 34-year-old man with ulcerative colitis, currently on mesalamine, is found to have abnormal liver enzyme levels on routine follow-up, as shown below.

He denies fevers, itching, abdominal pain, and weight loss. Viral hepatitis panel and autoimmune markers are normal. Right upper quadrant ultrasound is normal.

What is the best next test to evaluate liver test abnormalities?

- A. Computed tomography of abdomen
- B. Endoscopic ultrasound
- C. Endoscopic retrograde cholangiopancreatography
- D. Liver biopsy
- E. Magnetic resonance cholangiopancreatography

CORRECT ANSWER: E

RATIONALE

Magnetic resonance cholangiopancreatography (MRCP) is a noninvasive method to evaluate the biliary tree, a fluid-filled structure to evaluate for primary sclerosing cholangitis (PSC). It is equivalent in sensitivity and specificity to endoscopic retrograde cholangiopancreatography (ERCP), but without the risk of procedure-related pancreatitis. MRCP results are not affected by the serum bilirubin level (which is rate-limiting for radionuclide biliary scans). Computed tomography (CT) and endoscopic ultrasound (EUS) would be considered if pancreatic cancer was being considered as they are about equal in their utility for staging. CT is more useful than EUS for identifying liver and

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	245	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	106	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	76	10-40
Bilirubin, total, serum, mg/dL	0.8	0.3-1.0

other metastases. Liver biopsy would not be considered to evaluate large duct disease in PSC.

REFERENCES

Baillie J. Magnetic resonance cholangiopancreatography: the gastroenterologist's perspective. *Gastrointest Endosc.* 2002;55(7 Suppl):S13-S15. doi:10.1067/mge.2002.124750

Romagnuolo J, Bardou M, Rahme E, Joseph L, Reinhold C, Barkun AN. Magnetic resonance cholangiopancreatography: a meta-analysis of test performance in suspected biliary disease. *Ann Intern Med.* 2003;139(7):547-557. doi:10.7326/0003-4819-139-7-200310070-00006

Question 28

A 43-year-old woman with intermittent abdominal pain and loose stools undergoes an endoscopic retrograde cholangiopancreatography (ERCP) in the setting of an abnormal magnetic resonance CP (MRCP). Liver function test results are normal.

The fluoroscopic images from ERCP are shown below.



IMAGE COURTESY OF DUSHANT UPPAL, MD.

What intervention is most likely to provide long term benefit?

- A. Bile duct stent placement
- B. Cholecystectomy

- C. Colonoscopy
- D. Pancreatic sphincterotomy with stent placement
- E. Rectal indomethacin

CORRECT ANSWER: D

RATIONALE

The fluoroscopic image demonstrates anomalous pancreaticobiliary junction (APBJ). Patients with APBJ and a dilated common bile duct can often form stones in the common channel causing obstruction and related symptoms and the risk of pancreatitis. Long term benefit would be provided from pancreatic sphincterotomy with stent placement. Stent placement alone may only provide temporary relief. Cholecystectomy may not alleviate issues in the common bile duct. Colonoscopy would not resolve any biliary issues and would not be indicated as this image is not concerning for PSC. Rectal indomethacin would only be used to avoid pancreatitis in the post-ERCP setting and would not provide long term relief of this condition.

REFERENCE

Suchy SJ. Anatomy, histology, embryology, developmental anomalies and pediatric disorders of the biliary system. In: Feldman M, Friedman LS, and Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management, 8th ed.* Philadelphia: Elsevier; 2010:1182-1184.

Question 29

A 67-year-old woman with chronic heart failure and atrial fibrillation on warfarin was admitted with acute pancreatitis. Abdominal ultrasound demonstrates cholelithiasis and a common bile duct diameter of 6 mm without evidence of ascites. Recent echocardiogram demonstrated an ejection fraction of 45%. The patient is taking hydrochlorothiazide for her low ejection fraction. She states that her abdominal pain is improving.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	189	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	57	10-40
Bilirubin, total, serum, mg/dL	1.8	0.3-1.0
Hemoglobin, blood, g/dL	11	12-16
International normalized ratio	1.7	<1.1
Leukocyte (WBC) count, cells/ μ L	11,000	4000-11,000
Lipase, serum, U/L	153	10-140

Current laboratory results are above. Which of the following is the most appropriate management recommendation?

- A. Endoscopic ultrasonography
- B. Hydrochlorothiazide discontinuation
- C. Laparoscopic cholecystectomy
- D. Magnetic resonance cholangiopancreatography
- E. Nasoenteral tube feedings

CORRECT ANSWER: D

RATIONALE

Patients presenting with symptomatic cholelithiasis and biliary pancreatitis have an 18% to 31% risk of choledocholithiasis, thus falling in an intermediate (10%-50%) risk category. The bilirubin level greater than 1.8 mg/dL and normal common bile duct diameter also place this patient in the intermediate risk category. Patients at intermediate risk of choledocholithiasis benefit from further biliary evaluation before or during cholecystectomy but preferably with modalities that have a more favorable risk profile than endoscopic retrograde cholangiopancreatography (ERCP). These include endoscopic ultrasound, magnetic resonance cholangiopancreatography, intraoperative cholangiography, and intraoperative ultrasonography. Delays of 6 to 8 weeks to cholecystectomy are associated with unacceptable rates of recurrent biliary events (>35%). The patient has mild pancreatitis with improving pain that will allow oral intake soon; nasoenteral tube feeding has no role here. The improvement of pain also argues against hydrochlorothiazide being a cause of the pancreatitis which would only decrease with discontinuation of the drug. By any predictive scoring system, her

pancreatitis would be predicted mild. Although prolonged treatment (eg, 1 year) with ursodeoxycholic acid can dissolve a substantial proportion (approximately 50%) of cholesterol gallbladder stones, this is not a first-line therapy in the era of laparoscopic cholecystectomy and ERCP.

REFERENCE

ASGE Standards of Practice Committee, Buxbaum JL, Abbas Fehmi SM, et al. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. *Gastrointest Endosc.* 2019;89(6):1075-1105.e15. doi:10.1016/j.gie.2018.10.001

Question 30

A 67-year-old man with borderline resectable pancreatic cancer underwent an endoscopic retrograde cholangiopancreatography 2 months prior with placement of a plastic biliary stent and was subsequently started on chemotherapy. He now presents with fever, chills, right upper quadrant pain, and elevated liver function levels. A right upper quadrant ultrasound reveals mild intrahepatic biliary duct dilation and a distended, sludge-filled gallbladder. He is started on antibiotics.

What is the next best step in management?

- A. Cholecystectomy
- B. Endoscopic retrograde cholangiopancreatography (ERCP) with metal stent placement
- C. Magnetic resonance imaging of abdomen with cholangiopancreatography (MRCP)
- D. Percutaneous biliary drain placement
- E. Percutaneous gallbladder drainage

CORRECT ANSWER: B**RATIONALE**

The patient has cholangitis due to occlusion of the prior biliary stent. The appropriate treatment is urgent repeat endoscopic retrograde cholangiopancreatography with stent replacement. Cholecystectomy, biliary drain placement, and gallbladder drainage would not resolve the occluded stent and be more invasive than ERCP. MRCP would only provide diagnostic data, and this patient clinically is acutely ill and needing intervention.

REFERENCE

Sawas T, Al Halabi S, Parsi MA, Vargo JJ. Self-expandable metal stents versus plastic stents for malignant biliary obstruction: a meta-analysis. *Gastrointest Endosc.* 2015;82(2):256-267.e7. doi:10.1016/j.gie.2015.03.1980

Question 31

A healthy 43-year-old woman presents to the clinic as a referral from her primary care physician with intermittent abdominal pain. A right upper quadrant ultrasound demonstrates bile duct dilation to 12 mm. Her liver function test results are normal. You obtain magnetic resonance imaging, which demonstrates the findings below.

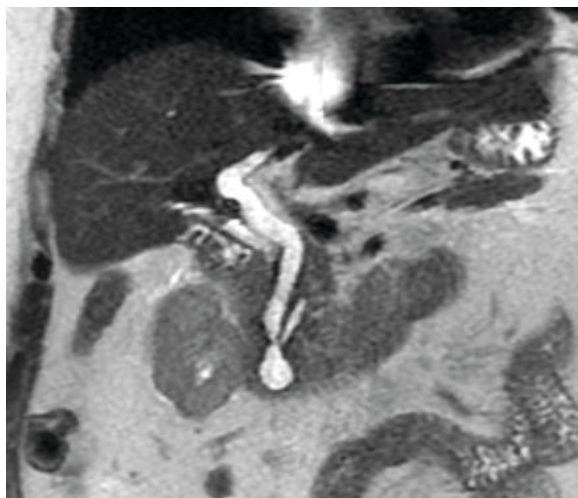


IMAGE COURTESY OF DUSHANT UPPAL, MD.

What is the next step in management?

- A. Cholecystectomy referral
- B. Continued observation
- C. Endoscopic ultrasound
- D. Endoscopic retrograde cholangiopancreatography with sphincterotomy
- E. Magnetic resonance cholangiopancreatography in 6 months

CORRECT ANSWER: D**RATIONALE**

The patient has a type 3 choledochal cyst. The appropriate management is endoscopic retrograde cholangiopancreatography with sphincterotomy to open the cyst and decrease risk of pancreatitis and malignancy. Cholecystectomy and observation would not alleviate the abdominal pain caused by the cyst nor remove the risk of development of biliary cancer. Endoscopic ultrasound and magnetic resonance cholangiopancreatography would be only diagnostic and not provide additional data than the imaging provided.

REFERENCE

Law R, Topazian M. Diagnosis and treatment of choledochoceles. *Clin Gastroenterol Hepatol.* 2014;12(2):196-203. doi:10.1016/j.cgh.2013.04.037

Question 32

A 27-year-old man with history of familial adenomatous polyposis treated with colectomy with short-segment rectal cuff and J-pouch is found to have an ampullary polyp on 6-month surveillance that has increased in size from 2 cm to 2.5 cm. Biopsies demonstrate adenoma with high-grade dysplasia (HGD) and a focus of intramucosal carcinoma. He has numerous additional duodenal polyps (Spigelman stage IV), several of which are greater than 1 cm in size, although none with HGD. Magnetic resonance cholangiopancreatography shows no evidence of intraductal polyp extension. The common bile duct measures 8 mm in diameter and pancreatic duct in the head of the pancreas measures 2 mm in diameter.

Laboratory results are notable for a total bilirubin level of 1.5 mg/dL (reference range, 0.3–1.0 mg/dL) but otherwise normal laboratory parameters.

What is the next most appropriate step in management?

- A. Endoscopic retrograde cholangiopancreatography and papillectomy with pancreas and bile duct stent placement
- B. Endoscopic retrograde cholangiopancreatography with sphincterotomy and bile duct stent placement
- C. Surgical referral for possible pancreaticoduodenectomy
- D. Surveillance endoscopy of ileoanal anastomosis and rectal cuff
- E. Surveillance upper endoscopy with endoscopic ultrasound in 6 months

CORRECT ANSWER: C

RATIONALE

Papillectomy in this instance is not recommended due to the presence of carcinoma in situ, multiple additional duodenal polyps, and the patient's young age. Endoscopic retrograde cholangiopancreatography without polyp resection is not recommended, as the lesion can be resected with likely cure given lack of evidence of malignancy. Due to significant growth of the ampullary adenoma along with HGD and carcinoma in situ, surveillance evaluation is not recommended.

Pancreaticoduodenectomy is the definitive treatment for ampullary adenomas with concern for early malignancy and possible obstruction in those patients deemed appropriate for surgery.

REFERENCES

Kim JH, Kim JH, Han JH, Yoo BM, Kim MW, Kim WH. Is endoscopic papillectomy safe for ampullary adenomas with high-grade dysplasia?. *Ann Surg Oncol*. 2009;16(9):2547-2554. doi:10.1245/s10434-009-0509-2

Offerhaus GJ, Giardiello FM, Krush AJ, et al. The risk of upper gastrointestinal cancer in familial adenomatous polyposis. *Gastroenterology*. 1992;102(6):1980-1982. doi:10.1016/0016-5085(92)90322-p

Question 33

A 62-year-old man with a history of chronic pancreatitis is evaluated for his level of pancreatic function by secretin stimulation testing. The presence of which of the following in the duodenum is the primary physiologic stimulus for secretin release into the blood?

- A. Acid
- B. Amino acids
- C. Carbohydrates
- D. Cholecystokinin
- E. Fat

CORRECT ANSWER: A

RATIONALE

The presence of acid in the duodenum stimulates mucosal endocrine cells there to secrete the hormone secretin into the blood that, in turn, stimulates the pancreatic centroacinar and ductal cells to secrete an alkaline pancreatic juice into the intestine to neutralize the acid and provide a pH at which pancreatic digestive enzymes and bile are effective. Amino acids and fat in the duodenum stimulate secretion of the hormone cholecystokinin by other duodenal endocrine cells, which helps stimulate secretion of digestive enzymes by the pancreatic acinar cells. The serine proteases (trypsin, chymotrypsin, elastase) among the pancreatic digestive enzymes exert a feedback inhibition of pancreatic secretion. Carbohydrates would stimulate the release of amylase and not secretin.

REFERENCES

Adler G, Nelson DK, Katschinski M, Beglinger C. Neurohormonal control of human pancreatic exocrine secretion. *Pancreas*. 1995;10(1):1-13. doi:10.1097/00006676-199501000-00001

Pandol SJ. Pancreatic physiology and secretory testing. In: Feldman M, Scharschmidt BF, Sleisenger MH, eds. *Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management*, 6th ed. Philadelphia: WB Saunders; 1998:771-782.

Question 34

A 28-year-old obese woman presents with the acute onset of epigastric abdominal pain, nausea, and vomiting. She consumes 1 to 2 glasses of wine 4 to 5 times weekly. She uses oral contraceptives. On physical examination, she is found to have diminished bowel sounds and epigastric tenderness.

Laboratory testing reveals the following results shown below.

Abdominal ultrasound shows a slightly enlarged pancreas with peripancreatic edema, several small gallbladder stones, and a common bile duct diameter of 6 mm.

What treatment would be the most likely to reduce risk of recurrent attacks?

- A. Alcohol cessation
- B. Cholecystectomy
- C. Contraceptive discontinuation
- D. Endoscopic retrograde cholangiopancreatography with sphincterotomy
- E. Prednisone treatment

CORRECT ANSWER: B

RATIONALE
The patient has gallstone pancreatitis as typified by elevation in bilirubin, liver transaminases, and alkaline phosphatase levels, all of which decreased over time. The risk of developing gallstone pancreatitis is affected by characteristics of the stones and gallbladder anatomy. Thus, risk increases with a larger cystic duct, increasing number of stones, and smaller stone size. Cholecystectomy is

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	332	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	82	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	88	85
Bilirubin, total, serum, mg/dL	3.6	0.3-1.0
Leukocyte (WBC) count, cells/ μ L	83,000	4000-11,000
Lipase, serum, U/L	781	10-140

One day later laboratory data are notable for the following results:

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	266	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	40	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	47	85
Bilirubin, total, serum, mg/dL	1.4	0.3-1.0
IgG4, serum, mg/dL	98	800-1500
Leukocyte (WBC) count, cells/ μ L	95,000	4000-11,000

the best option to reduce future attacks. Alcohol cessation would not reduce the risk from gallstones. Endoscopic retrograde cholangiopancreatography with sphincterotomy in the absence of a dilated common bile duct would be challenging. Contraceptive discontinuation and prednisone treatment would not alleviate the risk in the future from the stones present in the gallbladder.

REFERENCES

Armstrong CP, Taylor TV, Jeacock J, Lucas S. The biliary tract in patients with acute gallstone pancreatitis. *Br J Surg*. 1985;72(7):551-555. doi:10.1002/bjs.1800720718

Taylor TV, Armstrong CP. Migration of gall stones. *Br Med J (Clin Res Ed)*. 1987;294(6583):1320-1322. doi:10.1136/bmj.294.6583.1320

Question 35

A previously healthy, 62-year-old man presented 2 months ago with elevated liver function levels. An abdominal ultrasound and standard-protocol computed tomography scan of the abdomen revealed moderate intrahepatic biliary dilation and some gallbladder sludge. An endoscopic retrograde cholangiopancreatography revealed a stricture of the common hepatic duct with diffuse proximal biliary dilation. Cytologic brushings were obtained and ultimately returned negative for malignancy. A plastic stent was placed across the stricture. The patient returns for follow-up today, without complaint. Which is the best management option?

- A. Initiate ursodeoxycholic acid
- B. Obtain carcinoembryonic antigen level

- C. Perform magnetic resonance cholangiopancreatography
- D. Refer for cholecystectomy
- E. Repeat endoscopic retrograde cholangiopancreatography with brushing

CORRECT ANSWER: E

RATIONALE

Brushing has an approximately 50% yield. The overall picture is most consistent with a malignant biliary stricture. Repeat brushing and stent change is required. Initiating ursodeoxycholic acid or performing a Magnetic resonance cholangiopancreatography would not allow sampling of the bile duct cells. Cholecystectomy would allow examination of the gallbladder but not the common hepatic duct.

REFERENCE

Sherman S, Lehman GA. Endoscopic retrograde cholangiopancreatography, endoscopic sphincterotomy and stone removal, and endoscopic biliary and pancreatic drainage. In: Yamada T, ed. *Textbook of Gastroenterology*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2003:2866-2892.

Question 36

A 52-year-old woman underwent laparoscopic cholecystectomy for cholecystitis. She developed fevers with severe pain 6 days after the procedure and presents to the Emergency Department today. Computed tomography demonstrates a 5-cm fluid collection in the gallbladder fossa. Hepatobiliary iminodiacetic acid scanning is performed, demonstrating radiotracer uptake in the subhepatic space.

Laboratory results are as follows:

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	230	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	76	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	54	85
Bilirubin (total), serum, mg/dL	1.0	0.3-1.0
Leukocyte (WBC) count, cells/ μ L	21,000	4000-11,000

The next best step is:

- A. Endoscopic retrograde cholangiopancreatography with biliary sphincterotomy and stent placement
- B. Gram-positive antibiotic coverage
- C. Drainage of gall bladder fossa collection
- D. Percutaneous transhepatic biliary drain
- E. Surgical bile duct repair

CORRECT ANSWER: C

RATIONALE

The most appropriate management consists of drainage of the bile collection (biloma) due to concerns for infection, followed by placement of a short, large-caliber, transpapillary biliary stent to reduce the transsphincteric flow gradient. Antibiotic coverage should be Gram-negative, broad-spectrum coverage.

In this case the next best step is to drain the gall bladder fossa collection, then move onto sphincterotomy and stent placement.

This would avoid invasive surgery and the need for transhepatic drains.

REFERENCES

Abbas A, Sethi S, Brady P, Taunk P. Endoscopic management of postcholecystectomy biliary leak: When and how? A nationwide study. *Gastrointest Endosc.* 2019;90(2):233-241.e1. doi:10.1016/j.gie.2019.03.1173

Adler DG, Papachristou GI, Taylor LJ, et al. Clinical outcomes in patients with bile leaks treated via ERCP with regard to the timing of ERCP: a large multicenter study. *Gastrointest Endosc.* 2017;85(4):766-772. doi:10.1016/j.gie.2016.08.018

Abbas A et al. Endoscopic management of Lee CM, Stewart L, Way LW. Postcholecystectomy abdominal bile collections. *Arch Surg.* 2000;135(5):538-544. doi:10.1001/archsurg.135.5.538

Question 37

A 62-year-old overweight man with otherwise good health undergoes an abdominal ultrasound for an elevated alanine aminotransferase level. The ultrasound shows cholelithiasis with small gallstones, moderate hepatic steatosis, and a 14-mm gallbladder polyp.

What is the next step in management?

- A. Endoscopic ultrasound with fine needle aspiration
- B. Follow-up if symptoms develop
- C. Magnetic resonance imaging of abdomen with contrast
- D. Surgical referral for cholecystectomy
- E. Ultrasound in 6 months

CORRECT ANSWER: D

RATIONALE

Follow-up of gallbladder polyps less than 6 mm in diameter is not recommended in the absence of symptoms, signs, or laboratory abnormalities concerning for malignancy. With this 14mm polyp, the patient should be referred for possible surgery and removal. Endoscopic ultrasound, magnetic resonance imaging, and ultrasound would not fix the underlying risk of the gallbladder polyp, which needs to be removed.

REFERENCE

Andrén-Sandberg A. Diagnosis and management of gallbladder polyps. *N Am J Med Sci.* 2012;4(5):203-211. doi:10.4103/1947-2714.95897

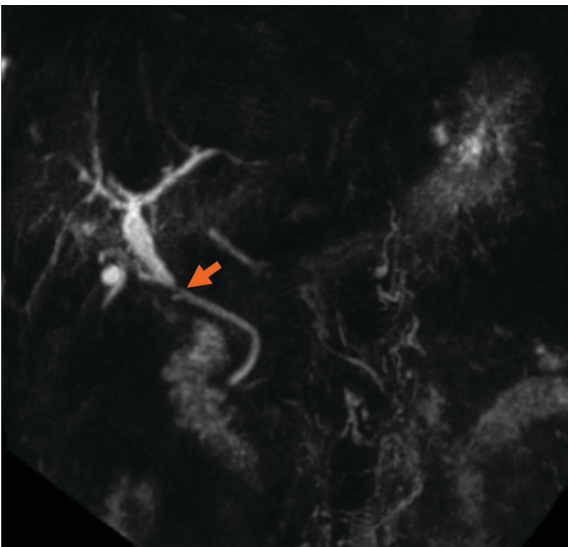
Question 38

A 62-year-old man who underwent orthotopic liver transplant 6 months ago for nonalcoholic steatohepatitis cirrhosis presents for clinic follow-up. He has been doing well, with previously normal liver enzyme levels.

Laboratory tests repeated at the clinic visit show the results on the following page.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	230	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	76	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	54	85
Bilirubin (total), serum, mg/dL	4.0	0.3-1.0
Total	3.1	0.1-0.3
Direct		

A magnetic resonance cholangiopancreatography is shown in the image below, with the area of interest marked with a red arrow.



Which is the most appropriate next step?

- A. Abdominal ultrasound with hepatic doppler
- B. Endoscopic retrograde cholangiopancreatography with stent placement
- C. Initiation of ursodeoxycholic acid
- D. Liver biopsy
- E. Surgical reconstruction

CORRECT ANSWER: B

RATIONALE

The patient has an anastomotic biliary stricture. These strictures occur most commonly in the first year after liver transplantation and can be managed endoscopically in most cases. For strictures that occur after the immediate post-transplantation period (>4 weeks after trans-

plantation), balloon dilation plus stent placement has been shown to be more effective than stent placement alone. Balloon dilation alone has no role. Surgical reconstruction is reserved for patients who fail endoscopic therapy, something that cannot be determined at the initial presentation. Ursodeoxycholic acid plays no therapeutic role in the management of this condition. Abdominal ultrasound with hepatic doppler and liver biopsy would not help to alleviate the biliary stricture and would be indicated if there was primary concern for transplanted organ rejection or hepatic artery thrombosis.

REFERENCES

Buxbaum JL, Biggins SW, Bagatelos KC, Ostroff JW. Predictors of endoscopic treatment outcomes in the management of biliary problems after liver transplantation at a high-volume academic center. *Gastrointest Endosc.* 2011;73(1):37-44. doi:10.1016/j.gie.2010.09.007

Schwartz DA, Petersen BT, Poterucha JJ, Gostout CJ. Endoscopic therapy of anastomotic bile duct strictures occurring after liver transplantation. *Gastrointest Endosc.* 2000;51(2):169-174. doi:10.1016/S0016-5107(00)70413-5

Question 39

A 42-year-old woman with chronic constipation and fibromyalgia is referred to the clinic for 2 years of intermittent postprandial right upper quadrant, “squeezing” abdominal pain with nausea and vomiting. She is taking adjusted dosing of an osmotic laxative and reports that she is having soft, formed stools daily. She has used topical heat therapy and occasional nonsteroidal anti-inflam-

matory drugs with some improvement in pain. An abdominal ultrasound is obtained demonstrating cholelithiasis without gallbladder wall thickening and with a common bile duct of 4 mm in diameter. Complete blood count and hepatic function panels are normal.

The most appropriate next step is:

- A. Cholecystectomy
- B. Hepatobiliary iminodiacetic acid scan
- C. Increased laxative use
- D. Pain management
- E. Ursodeoxycholic acid treatment

CORRECT ANSWER: A

RATIONALE

This patient has classic symptoms of biliary colic with evident cholelithiasis and should undergo cholecystectomy. A hepatobiliary iminodiacetic acid (HIDA) scan could be obtained if there were no structural etiologies (gallstones) seen on ultrasound. The patient has well managed constipation, and her pain has an etiology that can be treated. This is preferred rather than undertaking long-term pain management. Ursodeoxycholic acid may limit further stone formation in this patient, but she is young, and this strategy is unlikely to treat symptomatic cholelithiasis.

REFERENCE

Abraham S et al. Surgical and non-surgical management of gallstones. *Am Fam Physician*. 2014 May 15;89(10):795-802.

Question 40

A healthy, 72-year-old man presents with elevated liver function levels. An abdominal ultrasound demonstrates dilation of the common hepatic duct and intrahepatic bile ducts. Endoscopic retrograde cholangiopancreatography reveals a stricture of the common hepatic duct with diffuse proximal biliary dilation. Cytologic brushings are obtained, and a plastic stent is placed across the stenosis.

Repeat liver function tests show normal results, and cytology from bile duct stricture brushings demonstrates reactive cells.

What is the next best management option?

- A. Initiate ursodeoxycholic acid
- B. Obtain abdominal magnetic resonance imaging in 6 months
- C. Refer for surgical bile duct resection
- D. Repeat endoscopic retrograde cholangiopancreatography with brushing
- E. Schedule colonoscopy

CORRECT ANSWER: D

RATIONALE

Brushing has an approximately 50% yield. The overall picture is most consistent with a malignant biliary stricture in the absence of any gallstones. Repeat brushing and stent change is required to increase possible yield of malignant cells. Ursodeoxycholic acid initiation or colonoscopy would not help in the diagnosis or treatment of the hepatic duct stricture. Magnetic resonance imaging would not be as effective to evaluate the biliary system. Finally, surgical exploration would be much more invasive than repeated brushings.

REFERENCE

Sherman S, Lehman GA. Endoscopic retrograde cholangiopancreatography, endoscopic sphincterotomy and stone removal, and endoscopic biliary and pancreatic drainage. In: Yamada T, ed. *Textbook of Gastroenterology*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2003:2866-2892.

Question 41

A 76-year-old man with history of diabetes mellitus, stage 2 chronic kidney, coronary artery disease treated with coronary artery bypass graft, atrial fibrillation, and aortic stenosis treated with transarterial valve replacement 3 months ago is brought to the emergency department by his wife for 2 days of progressive right upper quadrant

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	430	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	320	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	234	10–40
Bilirubin, total, serum, mg/dL	2.8	0.3–1.0
Creatinine, serum, mg/dL	2.1 (1.5 at baseline)	0.7–1.5
International normalized ratio (INR)	2.6	< 1.1
Leukocyte (WBC) count, cells/ μ L	14,000	4000–11,000

(RUQ) abdominal pain, fevers, chills, and nausea. Upon examination, he is noted to be oriented only to person and appears jaundiced. He has tenderness to palpation in the RUQ without rebound. His blood pressure is 108/65 mmHg, heart rate is 110 bpm, and temperature is 39.2°C. Laboratory tests show the following results above.

RUQ ultrasound reveals a bile duct dilated to 12 mm and cholelithiasis.

The next best step in management is:

- A. Cholecystectomy
- B. Endoscopic retrograde cholangiopancreatography (ERCP) with stent placement
- C. Gram-positive antibiotic coverage
- D. Magnetic resonance cholangiopancreatography (MRCP)
- E. Percutaneous transhepatic biliary drain placement

CORRECT ANSWER: B

RATIONALE

The patient is suffering from acute cholangitis, demonstrated by the presence of Reynold's pentad. Cholangitis can be diagnosed by Charcot's triad (biliary obstruction, upper abdominal pain, and fever), but can progress onto Reynold's pentad (triad with confusion and hypotension). In this case clearance of the bile duct is of the utmost importance which is best accomplished with the ERCP and stent placement. Cholecystectomy may not clear the bile duct. The patient would require antibiotics but would need gram negative enteric coverage. MRCP would be diagnostic and not

therapeutic. Percutaneous biliary drain placement may be a last resort but can be associated with more complications than ERCP and stent placement, particularly with an elevated INR which increased bleeding risk.

REFERENCE

ASGE Standards of Practice Committee, Buxbaum JL, Abbas Fehmi SM, et al. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. *Gastrointest Endosc.* 2019;89(6):1075-1105.e15. doi:10.1016/j.gie.2018.10.001

Question 42

A 24-year-old man with abnormal liver enzyme levels undergoes endoscopic retrograde cholangiopancreatography, revealing the following result:

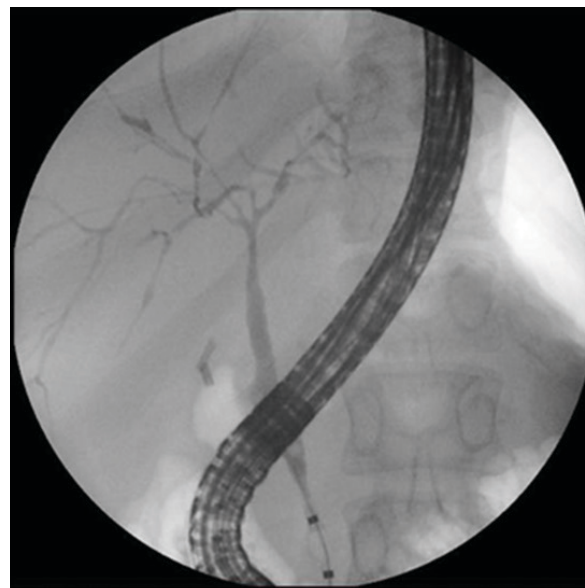


IMAGE COURTESY OF DUSHANT UPPAL, MD.

The next best step in management is:

- A. Bile duct stent placement
- B. Colonoscopy
- C. Corticosteroid therapy
- D. Liver transplantation referral
- E. Ursodeoxycholic acid therapy

CORRECT ANSWER: B

RATIONALE

This patient’s endoscopic retrograde cholangio-pancreatography shows typical changes of primary sclerosing cholangitis (PSC) limited to the intrahepatic ducts. He is likely to have inflammatory bowel disease. As this is often subclinical (asymptomatic), colonoscopy with random biopsies around the colon is an appropriate way to look for ulcerative colitis and Crohn’s disease. Ursodeoxycholic acid can be used for pruritus in PSC, but the patient does not have pruritus. Chenodeoxycholate is no longer used because of its history of causing liver injury. Corticosteroids have no role in the management of patients with PSC and may increase the risk of infection. Bile duct stenting is not needed as the imaging does not demonstrate a dominant stricture.

The patient does not demonstrate end-stage liver disease requiring liver transplantation referral at this time.

REFERENCES

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Chapman RW. Medical treatment of primary sclerosing cholangitis with ursodeoxycholic acid. *Dig Liver Dis*. 2003;35(5):306-308. doi:10.1016/s1590-8658(03)00072-0

Mendes FD, Lindor KD. Primary sclerosing cholangitis. *Clin Liver Dis*. 2004;8(1):195-211. doi:10.1016/S1089-3261(03)00127-2

Question 43

You are consulted about a 71-year-old woman admitted to the emergency department for a congestive heart failure exacerbation with computed tomography imaging demonstrating pneumobilia in the biliary tree and gallbladder and elevated liver enzyme levels. She has a remote history of endoscopic retrograde cholangiopancreatography for choledocholithiasis, coronary artery disease treated with coronary artery bypass grafting, and aortic stenosis. At admission, oxygen saturation was 85% on 5 L/min of supplemental oxygen by nasal cannula, and blood pressure was 65/45 mmHg with evidence of volume overload with an ejection fraction of 25% on echocardiogram. Furosemide was administered, resulting in diuresis. She had no tenderness on abdominal palpation. She is currently in the intensive care unit on 2 L/min of supplemental oxygen by nasal cannula. Her heart rate is 105 bpm, blood pressure is 100/65 mmHg, oxygen saturation is 95%, and temperature is 36.8°C.

Laboratory tests reveal the following results shown below.

The next best step is:

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	145	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	1300	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	1500	10-40
Bilirubin (total), serum, mg/dL	2.0	0.3-1.0
Leukocyte (WBC) count, cells/ μ L	11,000	4000-11,000

- A. Continued supportive cardiac care
- B. Endoscopic retrograde cholangiopancreatography with stent placement
- C. Intravenous antibiotics
- D. Percutaneous cholecystostomy tube placement
- E. Transhepatic biliary drain

CORRECT ANSWER: A

RATIONALE

The acute rise in liver transaminases suggest likely change due to ischemic hepatitis. The slight rise in bilirubin may suggest some congestive hepatopathy and the alkaline phosphatase is also only mildly elevated which goes against any severe obstruction. With the changes being due to the underlying cardiac disease, the most appropriate choice would be supportive cardiac care. Endoscopic retrograde cholangiopancreatography with stent placement is not indicated as there is no sign of obstruction.

Antibiotics are not needed with no sign of infection; the increased leukocyte count is likely due to reactionary change from the ischemic hepatitis.

REFERENCES

Seeto RK, Fenn B, Rockey DC. Ischemic hepatitis: clinical presentation and pathogenesis. *Am J Med.* 2000;109(2):109-113. doi:10.1016/S0002-9343(00)00461-7

Tapper EB, Sengupta N, Bonder A. The Incidence and Outcomes of Ischemic Hepatitis: A Systematic Review with Meta-analysis. *Am J Med.* 2015;128(12):1314-1321. doi:10.1016/j.amjmed.2015.07.033

Question 44

An 86-year-old man is admitted with right upper quadrant (RUQ) pain and vomiting. In the Emergency Department, vital signs are normal, and physical examination demonstrates mild RUQ tenderness. Complete blood count, comprehensive

metabolic panel, and lipase level are normal. RUQ ultrasound reveals multiple large gallstones with pneumobilia in the bile duct and gallbladder.

An abdominal radiograph demonstrates gastric and duodenal distention with air in the gallbladder.

What is the most likely diagnosis?

- A. Choledocholithiasis
- B. Cholecystoduodenal fistula
- C. Duodenal adenocarcinoma
- D. Emphysematous cholecystitis
- E. Perforated duodenal ulcer

CORRECT ANSWER: B

RATIONALE

This patient most likely has a cholecystoduodenal fistula (Bouveret's syndrome) due to fistulization of a large gallstone from the gallbladder into the adjacent duodenal bulb. This allows air to enter the gallbladder and adjacent bile ducts (if the cystic duct is patent). The "offending" gallstone may obstruct the lumen of the small bowel in the duodenum (causing gastric outlet obstruction) or beyond ("gallstone ileus"). Gallstones in the bile duct would be visualized on the ultrasound and would not cause duodenal distention. In emphysematous cholecystitis, the air is seen within the gallbladder wall, not within the lumen. A penetrating duodenal ulcer may occasionally fistulize into the gallbladder, but this is incredibly rare.

A duodenal carcinoma would not explain the pneumobilia in the bile duct and gallbladder.

REFERENCES

Marschall J, Hayton S. Bouveret's syndrome. *Am J Surg.* 2004;187(4):547-548. doi:10.1016/j.amjsurg.2003.12.031

Tan YM, Yeo AW, Wong CY. Multiple giant duodenal gallstones causing gastric outlet obstruction: Bouveret's minefield revisited. *Hepatogastroenterology.* 2003;50(54):1975-1977.

Question 45

You have been asked to perform an endoscopic retrograde cholangiopancreatography (ERCP) on a 76-year-old man recently admitted by his oncologist with progressive obstructive jaundice in the setting of a recently diagnosed head of pancreas cancer.

Vital signs are normal, and laboratory tests are notable for the following results shown at the bottom of the page.

The hospitalist informs you that the patient underwent port placement this morning with anesthesia and that they are planning for discharge tomorrow with urgent initiation of outpatient chemotherapy.

The patient is slightly somnolent but oriented to person, place, and time. He intermittently falls asleep as you are speaking with him about the procedure. The family states that the hospitalist has described the endoscopic ultrasound (EUS) and ERCP procedures, and they wish to proceed today. You ask them to describe the procedure and they say, “it involves a camera in the stomach.” The chart includes a paper consent form for endoscopy signed by the patient.

The next most appropriate steps to obtain consent for the accompanying EUS and ERCP is to:

- A. Discuss its risks in detail with patient while the family is present
- B. Ask the hospitalist to be present while consenting the patient and family
- C. Wait until the next day and then discuss the procedure with the patient and obtain consent

- D. Ensure the patient’s wife is the medical power of attorney then discuss the procedure with her
- E. Discharge the patient and reschedule in 1 week after patient has recovered from port placement

CORRECT ANSWER: C

RATIONALE

Although the diagnosis of pancreatic cancer requires urgent treatment, the patient has normal vital signs and is stable. For this scenario, it is important to ensure the patient has had time to clear any effects of the anesthesia. If the situation is not life threatening, the patient should be involved in these discussions. Relying on family, a hospitalist that is not doing the procedure, or a medical power of attorney should not be a strategy that is employed with this patient.

With a slightly elevated leukocyte count and bilirubin level of 14 mg/dL, the procedure being done the next day is likely better than waiting for 1 week.

REFERENCE

ASGE Standards of Practice Committee, Storm AC, Fishman DS, et al. American Society for Gastrointestinal Endoscopy guideline on informed consent for GI endoscopic procedures. *Gastrointest Endosc.* 2022;95(2):207-215.e2. doi:10.1016/j.gie.2021.10.022

Question 46

A 75-year-old woman with congestive heart failure (ejection fraction of 35%) and atrial fibrillation,

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	420	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	38	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	35	10-40
Bilirubin (total), serum, mg/dL	14	0.3-1.0
Leukocyte (WBC) count, cells/ μ L	12,000	4000-11,000

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	260	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	135	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	115	10–40
Bilirubin (total), serum, mg/dL	3.6	0.3–1.0

treated with rivaroxaban, is admitted with right upper quadrant abdominal pain and elevated liver function levels, as detailed above.

Abdominal ultrasound reveals a dilated bile duct and distended gallbladder.

During endoscopic retrograde cholangiopancreatography (ERCP) the following morning, biliary access proves to be difficult with eventual access obtained after 20 minutes. The pancreatic duct is wire cannulated several times before achieving bile duct access, with opacification demonstrating a normal, thin-caliber ventral duct.

A biliary sphincterotomy is performed with mild oozing. Cholangiogram and balloon sweep of the bile duct reveal microlithiasis and smooth tapering of the bile duct to the ampulla with no resistance to balloon passage. The cystic duct and gallbladder do not opacify. At the conclusion of the procedure, mild oozing is noted from the sphincterotomy site.

Which of the following would you recommend for treatment?

- A. Intravenous ketorolac tromethamine
- B. Short ventral pancreatic stent
- C. Uncovered metal biliary stent
- D. Urgent cholecystectomy
- E. Ventral pancreatic sphincterotomy

CORRECT ANSWER: B

RATIONALE

Prophylactic ventral pancreatic duct stents can reduce the risk of post-ERCP pancreatitis when cannulation difficulties or increased procedural

times occur, particularly if wire access to the ventral pancreatic duct is performed. Rectal indomethacin, but not intravenous ketorolac, has been shown to reduce post-ERCP pancreatitis. Uncovered metal biliary stents are indicated for malignant biliary strictures, which this patient does not have. The patient's distended gallbladder is likely due to common bile duct obstruction, which should be relieved with ERCP. Urgent cholecystectomy will not prevent post-ERCP pancreatitis. Ventral pancreatic sphincterotomy is unlikely to prevent post-ERCP pancreatitis and increases risk of pancreatitis development.

REFERENCES

- Elmunzer BJ, Scheiman JM, Lehman GA, et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. *N Engl J Med*. 2012;366(15):1414–1422. doi:10.1056/NEJMoa1111103
- Elton E, Howell DA, Parsons WG, Qaseem T, Hanson BL. Endoscopic pancreatic sphincterotomy: indications, outcome, and a safe stentless technique. *Gastrointest Endosc*. 1998;47(3):240–249. doi:10.1016/S0016-5107(98)70320-7
- Fazel A, Quadri A, Catalano MF, Meyerson SM, Geenen JE. Does a pancreatic duct stent prevent post-ERCP pancreatitis? A prospective randomized study. *Gastrointest Endosc*. 2003;57(3):291–294. doi:10.1067/mge.2003.124
- Sofuni A, Maguchi H, Itoi T, et al. Prophylaxis of post-endoscopic retrograde cholangiopancreatography pancreatitis by an endoscopic pancreatic spontaneous dislodgement stent. *Clin Gastroenterol Hepatol*. 2007;5(11):1339–1346. doi:10.1016/j.cgh.2007.07.008

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	185	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	29	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	35	10-40
Bilirubin, total, serum, mg/dL	0.8	0.3-1.0
Leukocyte (WBC) count, cells/ μ L	14,000	4000-11,000
Lipase, serum, U/L	180	10-140

Question 47

A 36-year-old woman undergoes endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy followed by papillary balloon dilation for large choledocholithiasis removal and plastic stent placement. In recovery, she reports severe pain radiating to her back that does not significantly improve with 2 doses of fentanyl. She is hemodynamically stable, but laboratory tests demonstrate the following results shown above.

A computed tomography scan of the abdomen is obtained demonstrating the following results:



Image obtained from: Simoes, Vitor & Magalhães, Sara & Faria, Gil & Silva, Donzília & Davide, José. (2014). Perforated Duodenal Diverticulum: Surgical Treatment and Literature Review. *International Journal of Surgery Case Reports*. 5. 10.1016/j.ijscr.2014.06.008.

The next most appropriate step in management is:

- A. Aggressive intravenous fluid for postprocedural pancreatitis
- B. Antibiotic treatment and observation
- C. Metal stent replacement of plastic stent
- D. Interventional radiology consult for percutaneous drain placement
- E. Surgical consult for emergent laparotomy

CORRECT ANSWER: C

RATIONALE

This patient has evidence of a type II duodenal perforation due to sphincterotomy with subsequent papillary dilation. Treatment would be to replace the plastic stent with a metal biliary stent to attempt to occlude the area of perforation. The elevated lipase is not necessarily a reflection of post ERCP pancreatitis and may be elevated due to surrounding inflammation from the perforation so intravenous fluid alone will not be enough for treatment. Antibiotics are appropriate, but observation is not. Percutaneous drain placement and emergent laparotomy should be reserved for when medical and endoscopic management fail.

REFERENCES

Howard TJ, Tan T, Lehman GA, et al. Classification and management of perforations complicating endoscopic sphincterotomy. *Surgery*. 1999;126(4):658-665.

Kumbhari V, Sinha A, Reddy A, et al. Algorithm for the management of ERCP-related perforations. *Gastrointest Endosc*. 2016;83(5):934-943. doi:10.1016/j.gie.2015.09.039

Question 48

A 65-year-old woman with prior history of choledocholithiasis treated with endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy and stone removal at 36 years of age presents with obstructive jaundice. She undergoes repeat ERCP, at which time a stricture in the mid common bile duct (CBD) is identified. Cytologic brushings are obtained that demonstrate reactive cells, and a single plastic stent is placed. She subsequently undergoes 2 further ERCPs for bile duct stent revision, with cytologic brushings repeated at each procedure demonstrating reactive atypia. During her last ERCP, 3 plastic stents are placed. She returns for repeat ERCP for stent removal. At the time of procedure, the previously identified mid-CBD stricture is noted to be improved.

The most appropriate next step is:

- A. Perform choledochoscopy with bile duct biopsies
- B. Place biliary stent
- C. Recommend close observation
- D. Repeat cytologic brushings
- E. Refer to surgery for consideration of extrahepatic bile duct resection

CORRECT ANSWER: A

RATIONALE

This patient has a refractory bile duct stricture that is likely benign. However, given the poor yield with cytologic brushings and prior evidence of atypia, choledochoscopy with bile duct biopsies should be performed for direct visualization and tissue sampling to ensure no evidence of malignancy. Replacing a biliary stent may be necessary to ensure ongoing biliary drainage, but this

should be done after choledochoscopy with biopsies. Repeat cytologic brushings are not indicated as they have been performed several times in the past and have been nondiagnostic. Surgical resection would be indicated in the setting of definitive malignancy but because of improvement in the biliary stricture, surgical resection for a recalcitrant benign bile duct stricture is not currently indicated.

REFERENCES

- Ramchandani M, Reddy DN, Gupta R, et al. Role of single-operator peroral cholangioscopy in the diagnosis of indeterminate biliary lesions: a single-center, prospective study. *Gastrointest Endosc.* 2011;74(3):511-519. doi:10.1016/j.gie.2011.04.034
- Shah RJ, Langer DA, Antillon MR, Chen YK. Cholangioscopy and cholangioscopic forceps biopsy in patients with indeterminate pancreaticobiliary pathology. *Clin Gastroenterol Hepatol.* 2006;4(2):219-225. doi:10.1016/s1542-3565(05)00979-1
- Sun X, Zhou Z, Tian J, et al. Is single-operator peroral cholangioscopy a useful tool for the diagnosis of indeterminate biliary lesion? A systematic review and meta-analysis. *Gastrointest Endosc.* 2015;82(1):79-87. doi:10.1016/j.gie.2014.12.021

Question 49

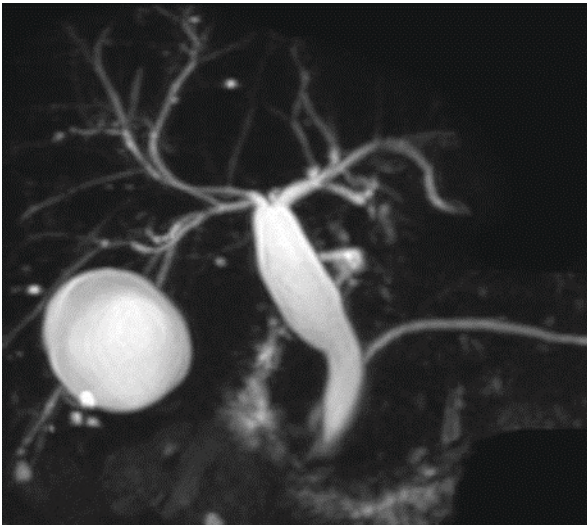
A 47-year-old overweight woman presents to the clinic with intermittent cramping and right upper quadrant abdominal pain.

Liver function tests have previously been performed, showing the following results:

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	115	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	65	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	41	10-40
Bilirubin, total, serum, mg/dL	0.7	0.3-1.0

Ultrasound is obtained with evidence of fat deposition within the liver. However, due to overlying bowel gas, the biliary tree cannot be adequately assessed.

You order magnetic resonance cholangiopancreatography, which demonstrates the findings below.



Source of image: Alexa Sasson, MD,
Maimonides Medical Center, Brooklyn, NY

The next best step in management is:

- A. Bile duct resection
- B. Cholecystectomy
- C. Endoscopic retrograde cholangiopancreatography with stent placement
- D. Liver biopsy
- E. Weight reduction counseling

CORRECT ANSWER: A

RATIONALE

This patient has a type I choledochal cyst and given the risk of development of cholangiocarcinoma, surgical cyst resection is recommended. Cholecystectomy and endoscopic retrograde cholangiopancreatography with stent placement will not remove the cyst or potential risk of cancer. The patient’s elevated liver function tests may be due to steatohepatitis, and weight reduction and/or liver biopsy may be indicated in the future if liver function tests remain elevated, but this is not the most appropriate next step in management.

REFERENCES

Stain SC, Guthrie CR, Yellin AE, Donovan AJ. Choledochal cyst in the adult. *Ann Surg.* 1995;222(2):128-133. doi:10.1097/00000658-199508000-00004

Todani T, Watanabe Y, Toki A, Urushihara N. Carcinoma related to choledochal cysts with internal drainage operations. *Surg Gynecol Obstet.* 1987;164(1):61-64.

Question 50

A 98-year-old man with cardiomyopathy (ejection fraction, 15%) and atrial fibrillation, on warfarin, admitted with fevers (temperature, 38.3 °C), chills, nausea, and right upper quadrant pain for 2 days is found to have the following laboratory results at the time of emergency department presentation are shown below. (Figure A)

Abdominal ultrasound reveals cholelithiasis with minimal gallbladder wall thickening,

Figure A

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	230	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	200	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	112	10-40
Bilirubin, total, serum, mg/dL	2.3	0.3-1.0
Creatinine, serum, mg/dL	1.2	0.7-1.5
International normalized ratio (INR)	2.0	<1.1
Leukocyte (WBC) count, cells/ μ L	15,000	4000-11,000

Figure B

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	315	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	275	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	180	10–40
Bilirubin, total, serum, mg/dL	3.6	0.3–1.0
Creatinine, serum, mg/dL	1.8	0.7–1.5
International normalized ratio (INR)	1.2	<1.1
Leukocyte (WBC) count, cells/ μ L	21,000	4000–11,000

choledocholithiasis, and a dilated common bile duct (diameter, 12 mm). His vital signs are stable at admission. He is started on intravenous piperacillin-tazobactam, given concern for cholangitis, and vitamin K.

Six hours later, he is noted to be febrile (temperature, 38.9 °C), tachycardic (heart rate, 115 bpm), and hypotensive (blood pressure, 85/55 mmHg) with repeat laboratory tests demonstrating the following results above. (Figure B)

He is given more intravenous fluid and started on low-dose vasopressor therapy with limited improvement in vitals.

Which of the following is the next best step?

- A. Change antibiotic therapy to meropenem
- B. Consult nephrology for continuous renal replacement therapy
- C. Perform endoscopic retrograde cholangiopancreatography with stent placement
- D. Place percutaneous transhepatic biliary drain
- E. Refer for emergent cholecystectomy

CORRECT ANSWER: D

RATIONALE

This patient has cholangitis with worsening laboratory parameters and hemodynamics despite initial resuscitative efforts and is thus unstable for anesthesia. Given improvement in INR, an emergent percutaneous transhepatic biliary drain should be placed. Although endoscopic retrograde cholangiopancreatography is the preferred

method for managing cholangitis, the patient's hemodynamic instability and already poor cardiac function place him at high risk of complications from anesthesia. Changing antibiotics may be necessary, but this will not treat the source of the infection and is not the next best step. The patient's worsening renal function is due to severe sepsis and thus treating the infection and continuing aggressive supportive care with intravenous fluids may aid in improving renal function; continuous renal replacement therapy is not currently indicated. The patient does not have cholecystitis and is not stable for anesthesia, so cholecystectomy is not indicated.

REFERENCE

ASGE Standards of Practice Committee, Buxbaum JL, Abbas Fehmi SM, et al. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. *Gastrointest Endosc.* 2019;89(6):1075-1105.e15. doi:10.1016/j.gie.2018.10.001

CHAPTER 5

Viral hepatitis

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Question 1

A 27-year-old pregnant woman presents to the clinic for counseling on therapy for chronic hepatitis C virus infection genotype 1a. Her pregnancy has been uneventful, and prenatal testing demonstrated negative HIV test and immunity from prior vaccination to hepatitis B virus. She did not start therapy and is inquiring about methods to reduce perinatal transmission. What is the best approach to perinatal care to reduce perinatal transmission of HCV?

- A. Advise against breastfeeding after delivery
- B. Avoid fetal scalp monitoring during gestation and delivery
- C. Recommend cesarean section at time of delivery
- D. Recommend therapy for her child immediately after delivery
- E. Start ledipasvir/sofosbuvir in the third trimester

CORRECT ANSWER: B**RATIONALE**

During pregnancy, patients with chronic hepatitis C virus infection should be monitored closely; however, antiviral therapy is not currently approved for the mother while pregnant or breastfeeding or for newborn infants. Patients should be followed up by a high-risk obstetrics team, and invasive monitoring should be avoided to reduce risk of transmission. Breastfeeding should only

be avoided if nipples are cracked, damaged, or bleeding. Therapy can be considered after delivery if patients are not breastfeeding, but viral load should be checked to assess for spontaneous clearance.

REFERENCES

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Society for Maternal-Fetal Medicine (SMFM). Electronic address: pubs@smfm.org, Hughes BL, Page CM, Kuller JA. Hepatitis C in pregnancy: screening, treatment, and management. *Am J Obstet Gynecol*. 2017;217(5):B2-B12. doi:10.1016/j.ajog.2017.07.039

Question 2

A 22-year-old Hispanic man presents to the emergency department with jaundice and abdominal pain. Clinical examination reveals no stigmata of chronic liver disease. The patient notes he works as an emergency medical technician and had a needle stick injury approximately 5 weeks ago for which he did not file a report or seek medical attention. He drinks 3 beers daily and more on the weekends. His history is notable for vaccination to hepatitis A virus and hepatitis B virus. Laboratory results are shown at the top on the following page.

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	1230	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	900	10-40
Bilirubin (total), serum, mg/dL	3.2	0.3-1.0
Hepatitis A IgM	Negative	Negative
Hepatitis B surface antibody	Positive	Negative
Hepatitis C antibody	Negative	Negative
Hepatitis core antibody IgM	Negative	Negative
Hepatitis surface antigen	Negative	Negative
Human immunodeficiency virus	Negative	Negative

Which of the following laboratory tests should you order next?

- A. Alcohol level
- B. Antinuclear antibodies
- C. Hepatitis A IgG
- D. Hepatitis C viral load by polymerase chain reaction
- E. Iron level

CORRECT ANSWER: D

RATIONALE

This patient’s clinical presentation—with elevated aminotransferases greater than 10 to 20 times the upper limit of normal in the setting of a possible high-risk exposure—make acute hepatitis C viral infection high in the differential diagnosis. He is vaccinated for hepatitis A and B viruses, and the serology are consistent with this. Antibodies to hepatitis C virus are not typically detectable until 8 weeks from exposure, and an evaluation of viral load is essential to establish the diagnosis.

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clinical presentation, laboratory findings and treatment outcomes. *Aliment Pharmacol Ther.* 2011;33(5):559-565. doi:10.1111/j.1365-2036.2010.04549.x

Maheshwari A, Ray S, Thuluvath PJ. Acute hepatitis C. *Lancet.* 2008;372(9635):321-332. doi:10.1016/S0140-6736(08)61116-2

Question 3

A 54-year-old man presents with new onset of rash with palpable purpura, visible non-blanching raised areas of the skin. He has a history of obesity, hypertension, and untreated chronic hepatitis C virus infection genotype 1b. He notes the rash is painful and has not responded to topical steroid therapy. He has also noted mild pitting lower extremity edema. Laboratory results are below. What is the next best step for therapeutic intervention?

- A. Daclatasvir/sofosbuvir plus ribavirin
- B. Elbasvir/grazoprevir
- C. Hemodialysis
- D. Intravenous immunoglobulin
- E. Oral prednisone 80 mg daily

Laboratory Test	Result	Reference Range
Protein (24 hour), urine, mg/24 hr	1300	<100
Aminotransferase, serum alanine (ALT, SGPT), U/L	68	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	54	10-40
Bilirubin (total), serum, mg/dL	1.2	0.3-1.0
Creatinine, serum, mg/dL	3.2	0.7-1.5
Cryoglobulins	Detectable	Negative
Hepatitis C virus, IU/L	100,450	Negative
Rheumatoid factor (nephelometry), IU/mL	92	<24

CORRECT ANSWER: B**RATIONALE**

This patient is presenting with essential mixed cryoglobulinemia. The skin involvement is classic. In the setting of elevated cryoglobulins, low complement levels, and renal disease, the diagnosis can be made clinically. The next best course of action is to treat underlying hepatitis C virus infection with a regimen approved for patients with renal dysfunction.

REFERENCES

Bruchfeld A, Roth D, Martin P, et al. Elbasvir plus grazoprevir in patients with hepatitis C virus infection and stage 4-5 chronic kidney disease: clinical, virological, and health-related quality-of-life outcomes from a phase 3, multicentre, randomised, double-blind, placebo-controlled trial. *Lancet Gastroenterol Hepatol*. 2017;2(8):585-594. doi:10.1016/S2468-1253(17)30116-4

Comarmond C, Garrido M, Pol S, et al. Direct-Acting Antiviral Therapy Restores Immune Tolerance to Patients With Hepatitis C Virus-Induced Cryoglobulinemia Vasculitis. *Gastroenterology*. 2017;152(8):2052-2062.e2. doi:10.1053/j.gastro.2017.02.037

Question 4

A 65-year-old man with hepatitis C virus infection genotype 1a underwent 12 weeks of therapy with subsequent sustained virologic response. Before therapy, an ultrasound demonstrated nodularity of the liver edge consistent with cirrhosis. Liver elastography findings are consistent with F4 fibrosis. The patient

returns to the clinic 6 months after starting therapy. Repeat HCV viral load remains negative, and additional laboratory tests are at the bottom of the page.

Which of the following should you do next?

- A. Esophagogastroduodenoscopy
- B. Fibroscan
- C. Hepatitis C viral load
- D. Liver biopsy
- E. Ultrasound

CORRECT ANSWER: E**RATIONALE**

This patient has well-compensated cirrhosis and has demonstrated sustained virologic response to therapy. Viral eradication has been shown to reduce risk of further hepatic decompensation. Although patients with early cirrhosis and sustained virologic response after therapy may have a relative lower risk of hepatocellular cancer, they still retain an overall increased risk and must undergo hepatocellular cancer surveillance indefinitely.

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Ioannou GN. HCC surveillance after SVR in patients with F3/F4 fibrosis. *J Hepatol*. 2021;74(2):458-465. doi:10.1016/j.jhep.2020.10.016

Kanwal F, Kramer J, Asch SM, Chayanupatkul M, Cao Y, El-Serag HB. Risk of Hepatocellular Cancer in HCV Patients Treated With Direct-Acting Antiviral Agents. *Gastroenterology*. 2017;153(4):996-1005.e1. doi:10.1053/j.gastro.2017.06.012

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	14	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	20	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0
Hemoglobin, blood, g/dL	14	Male: 14-18
Leukocyte count, cells/ μ L	8000	4000-11,000
Platelet count, plt/ μ L	160,000	150,000-450,000

Question 5

A 43-year-old woman with a 2-year history of chronic hepatitis C virus infection genotype 3 presents to the clinic to discuss treatment options. She has entered a substance abuse program and has stopped using intravenous drugs for the last 6 months. She has a normal ultrasound, and liver elastography demonstrates F1 fibrosis. She takes no medications. Urine pregnancy and HIV antibody tests are negative.

Which of the following should you do next?

- A. Elbasvir/grazoprevir for 12 weeks
- B. Hepatitis B serology
- C. Liver biopsy
- D. Sofosbuvir/velpatasvir for 12 weeks
- E. Urine drug screen

CORRECT ANSWER: B

RATIONALE

This patient is at high risk of coinfection with hepatitis B and C viruses and should be evaluated for hepatitis B virus infection before initiating therapy. Treatment with direct-acting antiviral therapy in the setting of coinfection with hepatitis B and C viruses might increase risk of reactivation and hepatitis.

REFERENCES

Chen G, Wang C, Chen J, et al. Hepatitis B reactivation in hepatitis B and C coinfecting patients treated with antiviral agents: A systematic review and meta-analysis. *Hepatology*. 2017;66(1):13-26. doi:10.1002/hep.29109

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Question 6

A 40-year-old woman presents with a history of compensated cirrhosis secondary to hepatitis C virus infection. She has a history of epilepsy, which is controlled with phenytoin. She has well-controlled hypertension managed with amlodipine. She is interested in direct-acting antiviral (DAA) therapy for treatment of hepatitis C virus infection.

What is the best plan for the chronic hepatitis C infection in this patient?

- A. Close observation
- B. Elbasvir/grazoprevir for 12 weeks
- C. Glecaprevir/pibrentasvir for 8 weeks
- D. Sofosbuvir/velpatasvir for 12 weeks
- E. Sofosbuvir/velpatasvir for 24 weeks

CORRECT ANSWER: A

RATIONALE

The patient is receiving anticonvulsant therapy, phenytoin, which is a cytochrome p450 (CYP) / P-glycoprotein (P-gp)-inducing agent and significantly lowers levels of all available DAA therapies. Assessment of all medication, including herbal supplements, before initiating DAA therapy in all patients is essential to avoid toxicity and ensure adequate therapeutic course. In this case, close observation would be the safest plan for this patient's hepatitis C infection.

REFERENCES

European Association for the Study of the Liver; Clinical Practice Guidelines Panel; et al. EASL recommendations on treatment of hepatitis C: Final update of the series*. *J Hepatol*. 2020;73(5):1170-1218. doi:10.1016/j.jhep.2020.08.018

University of Liverpool. HEP Drug Interactions. Interactions Checker. Accessed February 24, 2022. <https://www.hep-druginteractions.org/>

Question 7

A 43-year-old Vietnamese woman presents with a history of hepatitis C virus (HCV) infection genotype 4 without cirrhosis. She has never been treated. Her mother died of hepatocellular cancer secondary to hepatitis B virus (HBV) infection several years ago. A recent liver biopsy demonstrates chronic hepatitis with stage 1 fibrosis with positive HBV surface antigen staining. Ultrasound reveals a normal liver without hepatocellular cancer. Laboratory results are below. The patient inquires about initiating therapy. What is the next best step in management?

- A. Initiate direct-acting antiviral (DAA) therapy and start tenofovir after completion of 12 weeks of therapy
- B. Initiate DAA therapy with careful monitoring of HBV viral load and alanine aminotransferase
- C. Refer for liver transplantation
- D. Start tenofovir before initiating DAA therapy
- E. Start tenofovir and transition to DAA therapy when HBV viral load is under control

CORRECT ANSWER: D

RATIONALE

This patient has indications for HBV therapy and should be started on oral antiviral treatment before starting therapy for HCV infection. The US Food and Drug Administration

issued a black box warning for the use of DAA therapy in the setting of coinfection with actively replicating HBV due to risk of reactivation of HBV and hepatitis. Patients coinfecting with positive surface antigen and evidence of active replication should receive HBV therapy during treatment for HCV and at least 12 weeks after therapy with close monitoring.

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AASLD-IDSA. Monitoring Patients Who Are Starting HCV Treatment, Are on Treatment, or Have Completed Therapy. Recommendations for testing, managing, and treating hepatitis C. Accessed February 24, 2020.

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US Food and Drug Administration. FDA. FDA Drug Safety Communication: FDA warns about the risk of hepatitis B reactivating in some patients treated with direct-acting antivirals for hepatitis C. Drug and Safety Availability. October 4, 2016. Accessed February 24, 2022. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-about-risk-hepatitis-b-reactivating-some-patients-treated>

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	198	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	132	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0
Hepatitis B e-antibody	Positive	Negative
Hepatitis B e-antigen	Negative	Negative
Hepatitis B surface antibody	Negative	Negative
Hepatitis B viral load, IU/mL	3000	Negative
Hepatitis C viral load, IU/mL	130,245	Negative
Hepatitis core antibody IgG	Positive	Negative
Hepatitis surface antigen	Positive	Negative
Human immunodeficiency virus	Negative	Negative

Question 8

A 23-year-old White man presents to the clinic after being referred for a positive hepatitis C virus (HCV) antibody test with positive HCV viral load 8 months earlier. He continues to use intravenous drugs. Right upper quadrant ultrasound is normal, and liver elastography indicates F0 fibrosis. A repeat HCV viral load test remains positive. He is interested in therapy for HCV infection. He is HIV-negative and has been vaccinated for HBV. He has entered substance abuse counseling and participates in a needle exchange program. What is the next best course of action?

- A. Establish substance abuse contract with interval of sobriety before treatment
- B. Evaluate alcohol level
- C. Initiate treatment with direct-acting antiviral therapy
- D. Order urine drug screen
- E. Recommend against HCV therapy

CORRECT ANSWER: C

RATIONALE

Persons who inject illicit drugs are an important high-risk population, which should be targeted for screening for HCV infection and counseled on measures to reduce transmission. Active use of intravenous drugs is not a contraindication to therapy; therapy benefits the public health. After treatment and sustained virologic response, persons who inject illicit drugs should be screened for HCV reinfection with HCV RNA testing at least annually.

REFERENCES

Hellard M, Doyle JS, Sacks-Davis R, Thompson AJ, McBryde E. Eradication of hepatitis C infection: the importance of targeting people who inject drugs. *Hepatology*. 2014;59(2):366-369. doi:10.1002/hep.26623
Zelenev A, Mazhnaya A, Basu S, Altice FL. Hepatitis C virus treatment as prevention in

an extended network of people who inject drugs in the USA: a modelling study. *Lancet Infect Dis*. 2018;18(2):215-224. doi:10.1016/S1473-3099(17)30676-X

Question 9

A 42-year-old Black woman is listed for a heart transplant secondary to severe nonischemic cardiomyopathy. She is called in for the transplant and will receive a cardiac graft from a deceased hepatitis C virus (HCV) viremic donor. You are consulted to provide treatment recommendations. What is the best timing of therapy for HCV infection in this setting?

- A. After viremia is established in the recipient
- B. 6 months after transplantation
- C. 4-6 weeks after transplantation
- D. Immediately after transplantation

CORRECT ANSWER: D

RATIONALE

Treatment for HCV-negative recipients of nonliver organs from HCV-positive patients should begin immediately in the perioperative period at day 0 without waiting to confirm viral load positivity. Early therapy started preemptively with direct-acting antiviral therapy prevents development of chronic HCV infection and possible complications. Early reports indicate that treatment course may be shortened substantially with this strategy.

REFERENCES

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Woolley AE, Singh SK, Goldberg HJ, et al. Heart and Lung Transplants from HCV-Infected Donors to Uninfected Recipients. *N Engl J Med.* 2019;380(17):1606-1617. doi:10.1056/NEJMoa1812406

Question 10

A 65-year-old Black man with decompensated nonalcoholic steatohepatitis cirrhosis is listed for liver transplantation with a MELD (Model for End-Stage Liver Disease) score of 35. The patient is transplanted with a graft from a hepatitis C virus (HCV) viremic donor. His course was complicated by atrial fibrillation requiring amiodarone. A viral load and genotype are obtained at week 4 after transplantation revealing HCV genotype 1a. What is the best management plan after liver transplantation for the patient's HCV infection in this setting?

- A. Glecaprevir/pibrentasvir for 12 weeks
- B. Repeat viral load at 6 months to assess for spontaneous clearance
- C. Sofosbuvir/velpatasvir for 12 weeks
- D. Sofosbuvir/ledipasvir for 24 weeks
- E. Treatment is contraindicated after liver transplantation in this setting

CORRECT ANSWER: A

RATIONALE

Due to organ shortages and the advent of direct-acting antiviral therapy, centers are increasingly using HCV viremic donors for transplantation into HCV-negative recipients. Experience thus far indicates excellent outcomes; however, informed consent and counseling is essential. Early therapy within the first month is recommended when the patient is stable. Particular attention to drug interactions after transplantation is imperative as interactions, amiodarone in this case, require selection of specific drug secondary to interactions. Sofosbuvir and amiodarone should not be coadministered

REFERENCES

AASLD-IDSA. Treatment of HCV-Uninfected Transplant Recipients Receiving Organs From HCV-Viremic Donors. Recommendations for testing, managing, and treating hepatitis C. Accessed February 24, 2020. <https://www.hevguidelines.org/unique-populations/organs-from-hcv-viremic-donors>

Cotter TG, Paul S, Sandıkçı B, et al. Increasing Utilization and Excellent Initial Outcomes Following Liver Transplant of Hepatitis C Virus (HCV)-Viremic Donors Into HCV-Negative Recipients: Outcomes Following Liver Transplant of HCV-Viremic Donors. *Hepatology.* 2019;69(6):2381-2395. doi:10.1002/hep.30540

Kwong AJ, Wall A, Melcher M, et al. Liver transplantation for hepatitis C virus (HCV) non-viremic recipients with HCV viremic donors. *Am J Transplant.* 2019;19(5):1380-1387. doi:10.1111/ajt.15162

Question 11

A 53-year-old man presents with decompensated cirrhosis secondary to hepatitis C virus infection genotype 1b. He has ascites controlled with diuretics. He had an episode of esophageal variceal bleeding 6 months ago controlled with band ligation and nonselective beta blocker. His MELD (Model for End-Stage Liver Disease) score is 18, and his Child-Pugh score is C. He asks about pursuing hepatitis C virus treatment now. What is the best therapeutic option for this patient?

- A. Elbasvir/grazoprevir for 12 weeks
- B. Glecaprevir/pibrentasvir for 12 weeks
- C. Ombitasvir/paritaprevir/ritonavir/dasabuvir/ribavirin for 12 weeks
- D. Simeprevir/sofosbuvir/ribavirin for 12 weeks
- E. Sofosbuvir/ledipasvir for 24 weeks

CORRECT ANSWER: E

RATIONALE

For patients with decompensated Child-Pugh B/C cirrhosis regimens containing protease inhibitors are contraindicated due to hepatic metabolism and risk of drug-induced liver disease. In SOLAR-1, sustained virologic response rates were 86% in patients receiving 12 weeks of sofosbuvir/ledipasvir and 87% in patients receiving 24 weeks of sofosbuvir/ledipasvir. Treatment regimens should be based on a combination of sofosbuvir and an NS5A inhibitor (sofosbuvir/ledipasvir or sofosbuvir/velpatasvir). Addition of ribavirin, if tolerated, can shorten the duration of therapy.

REFERENCES

Charlton M, Everson GT, Flamm SL, et al. Ledipasvir and Sofosbuvir Plus Ribavirin for Treatment of HCV Infection in Patients With Advanced Liver Disease. *Gastroenterology*. 2015;149(3):649-659. doi:10.1053/j.gastro.2015.05.010

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Question 12

A 45-year-old woman underwent liver transplantation for decompensated hepatitis C virus (HCV) cirrhosis. Her posttransplantation course was complicated by seizures. She is currently receiving cyclosporine, mycophenolate mofetil, and prednisone. She has HCV genotype 3 and a viral load of 145,000 IU/mL. She has never been treated for HCV infection and is started on glecaprevir/pibrentasvir for 12 weeks. What is the most concerning result of drug interactions with this regimen?

- A. Decreased level of cyclosporine
- B. Decreased level of pibrentasvir

- C. Increased level of cyclosporine
- D. Increased level of glecaprevir

CORRECT ANSWER: D

RATIONALE

After liver transplantation, patients are often taking multiple medications, which may complicate HCV therapy. Cyclosporine has multiple interactions with direct-acting antiviral therapies; thus, careful consideration is essential when selecting regimens.

REFERENCES

AASLD-IDSA. Patients who develop recurrent HCV infection post liver transplantation. Recommendations for testing, managing, and treating hepatitis C. Accessed February 24, 2020. <https://www.hcvguidelines.org/unique-populations/post-liver-transplant>

European Association for the Study of the Liver; Clinical Practice Guidelines Panel; et al. EASL recommendations on treatment of hepatitis C: Final update of the series*. *J Hepatol*. 2020;73(5):1170-1218. doi:10.1016/j.jhep.2020.08.018

Question 13

A 65-year-old man underwent kidney transplantation with a kidney from a deceased, hepatitis C virus (HCV) viremic donor 6 weeks before presentation to the clinic. The patient has had a complicated postoperative course with severe organ rejection. He received thymoglobulin for induction. He presents to the clinic with complaint of jaundice but imaging results showing a normal liver. Laboratory results are listed on the following page.

What should you do next?

- A. Administer intravenous solumedrol
- B. Conduct liver biopsy
- C. Increase tacrolimus to goal level 10-12

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	140	140
Aminotransferase, serum aspartate (AST, SGOT), U/L	234	234
Bilirubin (total), serum, mg/dL	9	9
Cytomegalovirus	Undetectable	Undetectable
Epstein-Barr virus	Undetectable	Undetectable
Hepatitis B surface antibody	Positive	Positive
Hepatitis B viral load, IU/mL	Undetectable	Undetectable
Hepatitis C viral load, IU/mL	100,130,245	100,130,245
Hepatitis core antibody IgG	Positive	Positive
Hepatitis surface antigen	Negative	Negative

- D. Obtain magnetic resonance imaging of the liver
- E. Perform endoscopic retrograde cholangiopancreatography

CORRECT ANSWER: B

RATIONALE

This patient has fibrosing cholestatic HCV, which should be diagnosed by a combination of liver histology, clinical assessment, and HCV viral load assessment, which is typically high. This complication can occur in the setting of chronic HCV and is most closely associated with immunosuppression. It is typically associated with rapidly progressive cholestatic hepatitis and high HCV viral load. Diagnosis is made with histology, and treatment with direct-acting antiviral therapy can improve outcomes. Prompt recognition and therapy is essential. When suspicion exists, particularly in patients who have undergone liver transplantation, biopsy should always be obtained before starting empiric therapy for acute cellular rejection.

REFERENCES

European Association for the Study of the Liver; Clinical Practice Guidelines Panel; et

al. EASL recommendations on treatment of hepatitis C: Final update of the series*. *J Hepatol.* 2020;73(5):1170-1218. doi:10.1016/j.jhep.2020.08.018

Kapila N, Al-Khalloufi K, Bejarano PA, Vanatta JM, Zervos XB. Fibrosing cholestatic hepatitis after kidney transplantation from HCV-viremic donors to HCV-negative recipients: A unique complication in the DAA era. *Am J Transplant.* 2020;20(2):600-605. doi:10.1111/ajt.15583

Question 14

A 70-year-old Hispanic man presents to the clinic to discuss therapy for chronic hepatitis C virus infection genotype 1. He has F0-1 fibrosis on liver elastography. He has been treated with multiple prior direct-acting antiviral regimens in the past. His medications include insulin.

Laboratory results are below.

He is started on sofosbuvir/velpatasvir/voxilaprevir and ribavirin. With this regimen, the patient is at increased risk of developing which of the following?

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	198	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0
Hemoglobin, blood, g/dL	11	Male: 14-18
Hepatitis B surface antibody	Negative	Negative
Hepatitis core antibody	Negative	Negative
Hepatitis surface antigen	Negative	Negative
Human immunodeficiency virus	Negative	Negative

- A. Diabetic ketoacidosis
- B. Drug-induced liver injury
- C. Hemolytic anemia
- D. Hepatic encephalopathy
- E. Rhabdomyolysis

CORRECT ANSWER: C

RATIONALE

Ribavirin has important side effects with which clinicians must be familiar. In addition to teratogenicity, a dose-dependent hemolytic anemia is common; therefore, careful attention to initial dose and frequent monitoring of hemoglobin is essential. The dose should be limited in patients with renal insufficiency. Currently, ribavirin is used with both regimens for patients who have failed multiple direct-acting antiviral therapies. In the POLARIS-1 and POLARIS-4 trials, treatment with sofosbuvir/velpatasvir/voxilaprevir demonstrated high rates of sustained virologic response, and subsequent data support the use of ribavirin for extended 24-week courses of therapy.

REFERENCES

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Gane EJ, Shiffman ML, Etzkorn K, et al. Sofosbuvir-velpatasvir with ribavirin for 24 weeks in hepatitis C virus patients previously treated with a direct-acting antiviral regimen. *Hepatology*. 2017;66(4):1083-1089. doi:10.1002/hep.29256

Question 15

A 45-year-old Black man with hepatitis C virus (HCV) genotype 3 compensated cirrhosis presents to the clinic. He is treatment naive with no other comorbidities. He is

vaccinated against hepatitis A and hepatitis B viruses. Resistance testing is obtained, and the Y93H substitution is detected. Which of the following therapies is recommended?

- A. Elbasvir/grazoprevir
- B. Elbasvir/grazoprevir/ribavirin
- C. Sofosbuvir/ledipasvir
- D. Sofosbuvir/velpatasvir
- E. Sofosbuvir/velpatasvir/voxilaprevir

CORRECT ANSWER: E

RATIONALE

In patients with treatment-naïve HCV genotype 3 compensated cirrhosis, it is important to consider testing for resistance associated with Y93H substitution. Two options exist for this patient: sofosbuvir/velpatasvir/voxilaprevir or sofosbuvir/ledipasvir/ribavirin. In a study examining sofosbuvir/velpatasvir for HCV genotype 2+3 cirrhosis, sustained virologic response rates were 97% in the group without Y93H compared with 84% in the group with Y93H. Addition of ribavirin in a separate study improved sustained virologic response. Sofosbuvir/velpatasvir/voxilaprevir was studied in patients with HCV genotype 3 cirrhosis with sustained virologic response rates of 96%, and no effect of Y93H was found.

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Question 16

A 32-year-old woman with chronic hepatitis C virus (HCV) infection genotype 4 presents to the clinic to discuss treatment. She has a history of HIV and is receiving therapy. She exercises regularly and does not drink alcohol. She takes a statin for dyslipidemia. Liver elastography indicates F0 fibrosis. Her HCV viral load is 432,000 IU/mL.

What factor increases her risk of fibrosis progression?

- A. Dyslipidemia
- B. Genotype 4
- C. High viral load
- D. HIV coinfection

CORRECT ANSWER: D

RATIONALE

Several risk factors exist for progression of fibrosis including coinfection with HIV or hepatitis B virus. Viral load does not correlate with disease progression. Other risk factors include presence of fibrosis, older age, previous transplantation, alcohol consumption, obesity, and insulin resistance. Patients with HIV and HCV coinfection are at higher risk of fibrosis progression and should be targeted for screening and treatment.

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Konerman MA, Mehta SH, Sutcliffe CG, et al. Fibrosis progression in human immunodeficiency virus/hepatitis C virus coinfecting adults: prospective analysis of 435 liver biopsy pairs. *Hepatology*. 2014;59(3):767-775. doi:10.1002/hep.26741

Vogel M, Page E, Boesecke C, et al. Liver fibrosis progression after acute hepatitis C virus infection in HIV-positive individuals. *Clin Infect Dis*. 2012;54(4):556-559. doi:10.1093/cid/cir854

Question 17

A 63-year-old White man presents to the clinic to inquire about screening for reinfection with hepatitis C virus (HCV). He has previously been treated for chronic HCV infection 2 years ago with sustained virologic response. He periodically continues to use intravenous drugs with no plan to stop.

Which of the following tests should you order next?

- A. HCV antibody 1 time
- B. HCV antibody annually
- C. HCV genotype
- D. HCV-RNA polymerase chain reaction annually

CORRECT ANSWER: D

RATIONALE

Screening for HCV infection is now recommended one time in all people over the age of 18 years by the Centers for Disease Control and Prevention due to an increased incidence in younger cohorts. As HCV is a blood-borne pathogen, certain populations carry a higher risk of HCV infection and should be targeted for screening. Specific populations with higher-risk activities or exposures include intravenous drug users, men who have sex with men, intranasal illicit drug users, patients receiving hemodialysis, health care workers, children born to HCV-infected women, previously or currently incarcerated patients, patients with HIV infection, and patients who received blood transfusion or transplantation before July 1992. Once infected, HCV antibody testing will remain positive even in the setting of spontaneous clearance or treatment; therefore, monitoring with HCV-RNA polymerase chain reaction is recommended. In patients with persistent high-risk behaviors, annual screening is recommended.

REFERENCES

AASLD-IDSA. HCV Testing and Linkage to Care. Recommendations for testing, managing, and treating hepatitis C. Accessed February 24, 2020. <https://www.hcvguidelines.org/evaluate/testing-and-linkage>

Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC Recommendations for Hepatitis C Screening Among Adults - United States, 2020. *MMWR Recomm Rep*. 2020;69(2):1-17. Published 2020 Apr 10. doi:10.15585/mmwr.rr6902a1

Question 18

A 45-year-old Asian woman with chronic hepatitis C virus (HCV) infection genotype 1b presents to the clinic to discuss treatment. She was recently diagnosed with B-cell non-Hodgkin lymphoma and is likely to be treated with rituximab and chemotherapy. She is HIV- and HBV-negative. Which of the following should you do next?

- A. Liver ultrasound
- B. HCV treatment with direct-acting antiviral therapy
- C. Magnetic resonance imaging of abdomen
- D. Pegylated-interferon and ribavirin
- E. Close observation

CORRECT ANSWER: B

RATIONALE

There is a well-established association between chronic HCV infection and development of B-cell non-Hodgkin lymphoma. Prior studies demonstrated a decreased risk of lymphoma in patients successfully treated with interferon regimens. More recent data from a small study of 20 patients with HCV genotype 1b and diffuse large B-cell lymphoma suggests concurrent treatment with direct-acting antiviral therapy and chemotherapy was safe and effective. Given the relationship and likely

influence of HCV, treatment for chronic HCV infection in patients with non-Hodgkin lymphoma is recommended.

REFERENCES

Gisbert JP, García-Buey L, Pajares JM, Moreno-Otero R. Prevalence of hepatitis C virus infection in B-cell non-Hodgkin's lymphoma: systematic review and meta-analysis. *Gastroenterology*. 2003;125(6):1723-1732. doi:10.1053/j.gastro.2003.09.025

Persico M, Aglitti A, Caruso R, et al. Efficacy and safety of new direct antiviral agents in hepatitis C virus-infected patients with diffuse large B-cell non-Hodgkin's lymphoma. *Hepatology*. 2018;67(1):48-55. doi:10.1002/hep.29364

Question 19

A 56-year-old man with hepatitis C virus (HCV) infection genotype 1 without cirrhosis presents for routine follow-up 12 weeks after completing elbasvir/grazoprevir. His physical examination is normal, and he has been compliant with medications. HCV viral load is obtained and is negative. He has been vaccinated for hepatitis A and hepatitis B viruses.

What do you recommend to the patient next?

- A. Esophagogastroduodenoscopy for variceal screening
- B. Fibroscan yearly
- C. Follow-up as needed
- D. HCV viral load every 6 months
- E. Ultrasound in 6 months

CORRECT ANSWER: C

RATIONALE

Patients with a negative viral load at 12 weeks or longer after completion of therapy (sustained virologic response) are considered cured of HCV infection and needs follow up

only if needed. If a patient does not have cirrhosis or other liver-related risk factors, then they should be followed up the same as if they never had HCV per guideline recommendations. Longitudinal data from earlier treatment period with interferon and recent data with direct-acting antiviral therapy suggest patients remain free of HCV over the long term. Fibrosis can even improve after achieving sustained virologic response. Patients should be informed they can be reinfected in the future and encouraged to avoid risk factors.

REFERENCES

George SL, Bacon BR, Brunt EM, Mihindukulasuriya KL, Hoffmann J, Di Bisceglie AM. Clinical, virologic, histologic, and biochemical outcomes after successful HCV therapy: a 5-year follow-up of 150 patients. *Hepatology*. 2009 Mar;49(3):729-38. doi: 10.1002/hep.22694.

Manns MP, Pockros PJ, Norkrans G, et al. Long-term clearance of hepatitis C virus following interferon α -2b or peginterferon α -2b, alone or in combination with ribavirin. *J Viral Hepat*. 2013;20(8):524-529. doi:10.1111/jvh.12074

Sarrazin C, Isakov V, Svarovskaia ES, et al. Late Relapse Versus Hepatitis C Virus Re-infection in Patients With Sustained Virologic Response After Sofosbuvir-Based Therapies. *Clin Infect Dis*. 2017;64(1):44-52. doi:10.1093/cid/ciw676

Question 20

A 5-year-old adolescent girl acquired hepatitis C virus (HCV) infection genotype 4 at birth from her mother. She has had normal development without symptoms. She has a normal ultrasound and no other medical problems. She was vaccinated for HBV at birth and is HIV negative. She presents with her mother, and they inquire about treatment options.

What of the following should you do next?

- A. Deferred therapy until 18 years old
- B. Glecaprevir/pibrentasvir
- C. Ledipasvir/sofosbuvir
- D. Pegylated-interferon and ribavirin
- E. Repeat HCV viral load yearly

CORRECT ANSWER: C

RATIONALE

Several direct-acting antiviral (DAA) regimens are now approved for use in children. To date, ledipasvir/sofosbuvir is the only DAA therapy approved for patients 3 years of age or older. Trials have shown high rates of efficacy of DAA therapy with sustained virologic response rates similar to those of the adult population. Two other DAA therapies are approved for children (sofosbuvir/velpatasvir for patients ≥ 6 years of age and glecaprevir/pibrentasvir for patients ≥ 12 years of age). As liver disease and fibrosis risk progresses over time, therapy is now indicated in children with chronic HCV infection. Although complications of HCV such as cirrhosis are rare in childhood, studies have shown that treatment is cost-effective and reduces potential of transmission and risk of liver disease progression.

REFERENCES

Indolfi G, Easterbrook P, Dusheiko G, et al. Hepatitis C virus infection in children and adolescents. *Lancet Gastroenterol Hepatol*. 2019;4(6):477-487. doi:10.1016/S2468-1253(19)30046-9

Nguyen J, Barritt AS 4th, Jhaveri R. Cost Effectiveness of Early Treatment with Direct-Acting Antiviral Therapy in Adolescent Patients with Hepatitis C Virus Infection. *J Pediatr*. 2019;207:90-96. doi:10.1016/j.jpeds.2018.12.012

Schwarz KB, Rosenthal P, Murray KF, et al. Ledipasvir-Sofosbuvir for 12 Weeks in Children 3 to <6 Years Old With Chronic Hepa-

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	234	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	290	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0
Leukocyte count, cells/uL	1200	4000-11,000

titis C. *Hepatology*. 2020;71(2):422-430.
doi:10.1002/hep.30830

Question 21

A 57-year-old Black woman recently underwent liver transplantation for hepatitis C cirrhosis 5 months ago. The donor cytomegalovirus (CMV) IgG was positive, and the recipient IgG was negative. She presents to the clinic with complaint of fever, diarrhea, and fatigue. She is compliant with her immunosuppression. Laboratory results are shown above. A liver biopsy is obtained and shows viral inclusions and microabscesses. Which of the following should you do next?

- A. Cytomegalovirus viral load testing
- B. Empiric high-dose steroids
- C. Hepatitis B viral load testing
- D. Magnetic resonance imaging of the liver

CORRECT ANSWER: A

RATIONALE

The presence of fever, leukopenia, and systemic symptoms are associated with CMV disease. CMV is a common infection after liver transplantation in the first 6 months. CMV can affect multiple organs including the lungs, gastrointestinal tract, and liver. This patient has a high-risk profile with CMV-positive donor/CMV-negative recipient. The liver biopsy suggests features consistent with tissue-invasive disease, and an evaluation of CMV viral load would be the next step before initiating treatment to assist with monitoring while treating with valganciclovir. Strategies to monitor for CMV infection include antiviral prophylaxis or monitoring of CMV viral load and initiating preemptive therapy. A recent randomized

controlled trial compared preemptive therapy versus antiviral prophylaxis in seronegative liver transplant recipients and found lower rates of CMV disease with preemptive therapy.

REFERENCES

Razonable RR, Hayden RT. Clinical utility of viral load in management of cytomegalovirus infection after solid organ transplantation. *Clin Microbiol Rev*. 2013;26(4):703-727. doi:10.1128/CMR.00015-13

Razonable RR, Humar A. Cytomegalovirus in solid organ transplant recipients—Guidelines of the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;33(9):e13512. doi:10.1111/ctr.13512

Singh N, Winston DJ, Razonable RR, et al. Effect of Preemptive Therapy vs Antiviral Prophylaxis on Cytomegalovirus Disease in Seronegative Liver Transplant Recipients With Seropositive Donors: A Randomized Clinical Trial. *JAMA*. 2020;323(14):1378-1387. doi:10.1001/jama.2020.3138

Question 22

A 23-year-old woman presents to her local emergency department with confusion. On examination she is noted to be febrile with altered mental status and asterixis. Her past medical history includes a recent diagnosis of lymphoma, and she is currently undergoing treatment with chemotherapy. Her laboratory results are at the top of the following page.

Imaging with ultrasound demonstrates a normal appearing liver without vascular or biliary abnormalities. Which of the following therapies should you order?

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	86	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	4510	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	5670	10-40
Bilirubin (total), serum, mg/dL	1.6	0.3-1.0
International normalized ratio	4.5	<1.1

- A. Acyclovir
- B. Mannitol
- C. Oseltamivir
- D. Prednisone
- E. Rifaximin

CORRECT ANSWER: A

RATIONALE

Herpes simplex virus can cause severe hepatitis and acute liver failure that is highly fatal. Prompt recognition and early therapy with acyclovir is essential. Diagnosis is challenging as the disease is rapidly progressive. Immuno-compromised patients and women in the third trimester of pregnancy are most affected; however, immunocompetent individuals may also be affected. Herpes simplex virus skin lesions are not always present, and characteristic features on laboratory tests include significantly elevated transaminases and typically low bilirubin level.

REFERENCE

Norvell JP, Blei AT, Jovanovic BD, Levitsky J. Herpes simplex virus hepatitis: an analysis of the published literature and institutional cases. *Liver Transpl.* 2007;13(10):1428-1434. doi:10.1002/lt.21250

Question 23

An 18-year-old woman was referred after undergoing evaluation for acute pharyngitis,

fever, and malaise. An abdominal ultrasound reveals normal liver contours and parenchyma with mild splenomegaly. Physical examination is unremarkable except for cervical adenopathy. Laboratory results are shown below. What is the best treatment plan for this patient?

- A. Close observation
- B. Hepatitis A IgM testing
- C. Hepatitis B core IgM testing
- D. Liver biopsy
- E. Liver magnetic resonance imaging

CORRECT ANSWER: A

RATIONALE

This patient has clinical characteristic features of infectious mononucleosis, which is typically caused by Epstein-Barr virus (EBV). This can be diagnosed clinically when patients present with a constellation of symptoms including fever, pharyngitis, adenopathy, and fatigue. Laboratory testing to evaluate for atypical lymphocytes and heterophile testing (eg, monospot) will establish the diagnosis. Liver enzymes are very commonly elevated and resolve without intervention and only require close observation to ensure they resolve. Splenomegaly is common, and patients should be counseled on risk of spleen rupture and avoiding contact sports. The differential diagnosis includes acute HIV infection, cytomegalovirus-related disease, and other infections.

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	287	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	200	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0
Leukocyte count, cells/uL	6800; presence of atypical lymphocytes on differential	4000-11,000
Monospot	Positive	Negative

Monospot may be negative in early disease, and evaluation with EBV serology is indicated if suspicion is high. In EBV-negative disease, expanding the workup with cytomegalovirus IgM and HIV testing is recommended.

REFERENCES

Kofteridis DP, Koulentaki M, Valachis A, et al. Epstein Barr virus hepatitis. *Eur J Intern Med.* 2011;22(1):73-76. doi:10.1016/j.ejim.2010.07.016

Linderholm M, Boman J, Juto P, Linde A. Comparative evaluation of nine kits for rapid diagnosis of infectious mononucleosis and Epstein-Barr virus-specific serology. *J Clin Microbiol.* 1994;32(1):259-261. doi:10.1128/jcm.32.1.259-261.1994

Vine LJ, Shepherd K, Hunter JG, et al. Characteristics of Epstein-Barr virus hepatitis among patients with jaundice or acute hepatitis. *Aliment Pharmacol Ther.* 2012;36(1):16-21. doi:10.1111/j.1365-2036.2012.05122.x

Question 24

A 72-year-old White woman without prior liver disease is hospitalized with respiratory failure secondary to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. She is receiving oxygen and is normotensive. The patient is receiving steroids and ceftriaxone but no other medications currently and no herbal supplements. Right upper quadrant ultrasound reveals a normal-appearing liver with no biliary dilation. Laboratory results are below. What is the best treatment plan for this patient?

- A. Close observation
- B. Epstein-Barr viral load testing
- C. Endoscopic retrograde cholangiopancreatography
- D. Hepatitis E IgM testing
- E. Liver biopsy

CORRECT ANSWER: A

RATIONALE

Elevation in aminotransferases is commonly seen in patients infected with SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19). This patient’s laboratory tests are consistent with a pattern typically seen in COVID-19, and assessment with invasive testing or of less likely viral causes is not indicated. The typical pattern of elevation is isolated to alanine and aspartate aminotransferases and usually less than 5 times the upper limit of normal; however, total bilirubin and alkaline phosphatase levels can be elevated. Patients with elevated liver enzymes and no preexisting liver disease should be assessed for alternative explanations as clinically appropriate. Often patients have coexisting risk factors and careful assessment of medications (eg, remdesivir) for drug-induced liver injury is important. A severe liver injury characterized by cholangiopathy has also been associated with SARS-CoV-2 infection.

REFERENCES

Bertolini A, van de Peppel IP, Bodewes FAJA, et al. Abnormal Liver Function Tests in Patients With COVID-19: Relevance and Potential Pathogenesis. *Hepatology.* 2020;72(5):1864-1872. doi:10.1002/hep.31480

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	140	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	185	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	190	10-40
Bilirubin (total), serum, mg/dL	1.5	0.3-1.0
Hepatitis A virus	Negative	Negative
Hepatitis B virus	Negative	Negative
Hepatitis C virus	Negative	Negative

Faruqui S, Okoli FC, Olsen SK, et al. Chol-angiopathy After Severe COVID-19: Clinical Features and Prognostic Implications. *Am J Gastroenterol*. 2021;116(7):1414-1425. doi:10.14309/ajg.0000000000001264

Montastruc F, Thuriot S, Durrieu G. Hepatic Disorders With the Use of Remdesivir for Coronavirus 2019. *Clin Gastroenterol Hepatol*. 2020;18(12):2835-2836. doi:10.1016/j.cgh.2020.07.050

Question 25

A 23-year-old Black man presents to the clinic with complaint of fever, cough, malaise, and sore throat. His symptoms have been ongoing for approximately 2 weeks. He has no past medical history and is otherwise healthy. He has no recent travel and denies contact with sick persons. He is vaccinated for hepatitis A and B viruses. Computed tomography of the abdomen is normal. Laboratory results are below.

What diagnostic test is indicated now?

- A. Blood cultures
- B. Ceruloplasmin
- C. Cytomegalovirus IgM
- D. Hepatitis E viral load

CORRECT ANSWER: C

RATIONALE

Cytomegalovirus (CMV) infection in the immunocompetent host is common worldwide, and incidence increases with age. The manifestations of primary CMV infection or reactivation of prior infection include specific organ complications, which may affect the gastrointestinal tract, liver, lungs, eyes, and central nervous system. Symptoms may overlap considerably with presentation of Epstein-Barr virus mononucleosis. Presentation later in life may represent reactivation of prior infection due to immunosuppressed state or infection with novel strain of virus. Abnormal liver enzymes in CMV infection are very common, and multiple case reports of severe hepatitis have been reported.

Other associations of CMV include granulomatous hepatitis, cholestatic liver injury, and portal vein thrombosis. Treatment is generally supportive care; however, in some cases, use of antiviral therapies, such as valganciclovir, have been reported.

REFERENCES

Burkey C, Teng C, Hussein KI, Sabetta J. Cytomegalovirus (CMV)-associated portal vein thrombosis in a healthy, immunocompetent man. *BMJ Case Rep*. 2020;13(12):e238645. Published 2020 Dec 28. doi:10.1136/bcr-2020-238645

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	398	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	268	10-40
Bilirubin (total), serum, mg/dL	1.0	0.3-1.0
Epstein-Barr virus antibodies	Negative	Negative
Hepatitis A virus IgM	Negative	Negative
Hepatitis B surface antibody	Positive	Negative
Hepatitis C viral load	Undetected	Negative
Hepatitis core antibody	Negative	Negative
Hepatitis surface antigen	Negative	Negative
Human immunodeficiency virus (HIV) antibody	Negative	Negative
HIV viral load	Undetected	Negative
Leukocyte count, cells/uL	10,000; atypical lymphocytes on differential	Negative
Monospot	Negative	Negative

Fernández-Ruiz M, Muñoz-Codoceo C, López-Medrano F, et al. Cytomegalovirus myopericarditis and hepatitis in an immunocompetent adult: successful treatment with oral valganciclovir. *Intern Med*. 2008;47(22):1963-1966. doi:10.2169/internalmedicine.47.1480

Staras SA, Dollard SC, Radford KW, Flanders WD, Pass RF, Cannon MJ. Seroprevalence of cytomegalovirus infection in the United States, 1988-1994. *Clin Infect Dis*. 2006;43(9):1143-1151. doi:10.1086/508173

Zahid M, Ali N, Saad M, Kelly P, Ortiz A. Acute Cytomegalovirus (CMV) Hepatitis in an Immunocompetent Adult. *Am J Case Rep*. 2020;21:e925495. Published 2020 Jul 16. doi:10.12659/AJCR.925495

Question 26

A 72-year-old woman presents to clinic after having elevated liver test results. She has been in her usual state of health over the last year without jaundice or abdominal pain. On examination, her liver is normal size, and she does not have right upper quadrant tenderness. She has not been vaccinated for hepatitis A or B in the past.

Laboratory results are below.

What is your next step in management?

- A. Vaccinate for hepatitis A/hepatitis B
- B. Administer hepatitis A virus immunoglobulin

- C. Counsel patient that household contacts should be told she may have been recently exposed to hepatitis A virus
- D. Obtain Doppler liver ultrasound
- E. Obtain serum iron studies

CORRECT ANSWER: E

RATIONALE

This patient is asymptomatic currently, despite elevations of liver test results; thus, the positive IgM for hepatitis A virus is likely a false positive. Most adults are symptomatic from hepatitis A virus. Her liver test results are mildly elevated and would necessitate further investigation of elevated liver test results with iron studies. Ultrasound with dopplers is not indicated as the elevation of liver test results is not sufficiently high.

REFERENCES

Centers for Disease Control and Prevention (CDC). Positive test results for acute hepatitis A virus infection among persons with no recent history of acute hepatitis--United States, 2002-2004. *MMWR Morb Mortal Wkly Rep*. 2005;54(18):453-456.

Kwo PY, Cohen SM, Lim JK. ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. *Am J Gastroenterol*. 2017;112(1):18-35. doi:10.1038/ajg.2016.517

Question 27

A 66-year-old Black man, with a new diagnosis of alcohol-associated liver disease and cirrhosis that is well compensated, presents

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	156	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	110	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	94	10-40
Bilirubin (total), serum, mg/dL	0.5	0.3-1.0
Hepatitis A IgG	Positive	Negative
Hepatitis A IgM	Positive	Negative
Hepatitis C antibody	Negative	Negative
Hepatitis surface antigen	Negative	Negative

to clinic before travel to Southeast Asia for business travel. His liver test results are normal, but you discover that he is not immune to hepatitis A virus (HAV). He is leaving for Southeast Asia in 2 months.

What is your recommendation with regard to prevention of HAV infection?

- A. Give 1 dose of HAV vaccine now
- B. Give 1 dose of HAV vaccine with 1 dose of immunoglobulin now
- C. Give 1 dose of HAV vaccine now and 1 dose of HAV vaccine in 6 months
- D. Give 1 dose of HAV vaccine with 1 dose of immunoglobulin now and 1 dose of HAV vaccine in 6 months
- E. Give 2 doses of HAV vaccine now

CORRECT ANSWER: B

RATIONALE

Patients with chronic liver disease have lower rates of response to the HAV vaccine overall. Before travel, healthy patients over the age of 40 and patients with more than 6 months of immune compromise or with chronic liver disease should receive 1 dose of HAV vaccination with 1 dose of immunoglobulin as pre-exposure prophylaxis.

REFERENCE

Nelson NP, Weng MK, Hofmeister MG, et al. Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020. *MMWR Recomm Rep.* 2020;69(5):1-38. Published 2020 Jul 3. doi:10.15585/mmwr.rr6905a1

Question 28

You are seeing a 45-year-old woman with a hepatic adenoma for the first time. She is well prepared for her clinic visit and has her medical history and vaccination records avail-

able. She got 1 dose of the hepatitis A vaccine 2 years ago when she was at her prior job in another city. She asks you what she should do about her hepatitis A vaccine series.

What is your recommendation?

- A. Give 1 dose of HAV vaccine now
- B. Give 1 dose of HAV vaccine now and 1 dose of HAV vaccine in 6 months
- C. Give 1 dose of HAV vaccine with 1 dose of immunoglobulin now and 1 dose of HAV vaccine in 6 months
- D. Give 1 dose of HAV vaccine with 1 dose of immunoglobulin now
- E. Give 2 doses of HAV vaccine now

CORRECT ANSWER: A

RATIONALE

If only 1 HAV vaccine dose is given and the series is not completed, it can be continued with the second dose rather than restarting the series. Immunoglobulin is not indicated for routine vaccination.

REFERENCE

Nelson NP, Weng MK, Hofmeister MG, et al. Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020. *MMWR Recomm Rep.* 2020;69(5):1-38. Published 2020 Jul 3. doi:10.15585/mmwr.rr6905a1

Question 29

A 58-year-old man presents with fatigue, abdominal pain, fever, and jaundice over the course of 1 week. He was diagnosed with hepatitis A virus (HAV) after HAV IgM tests returned positive. He was admitted to the hospital and was discharged after 3 days. He then presents to the urgent care 6 weeks later with low grade fever, itching, and worsening jaundice. Before hospitalization, patient had

Laboratory Test	Result	Follow-up Result	Reference Range
Alkaline phosphatase, serum, U/L	276	396	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	5780	211	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	4732	205	10-40
Bilirubin (total), serum, mg/dL	2.1	28.9	0.3-1.0

been drinking 6 drinks a week and taking ibuprofen as needed for fever. Laboratory results are above.

What is the next best step in management?

- A. Broad spectrum antibiotics
- B. N-acetylcysteine
- C. Thiamine and folate
- D. Liver biopsy
- E. Cholestyramine

CORRECT ANSWER: E

RATIONALE

Hepatitis A can present with a prolonged cholestatic course, relapsing HAV infection, with jaundice lasting several weeks to months after initial infection. Liver biopsy is unlikely to be helpful in diagnosis as HAV-induced autoimmune hepatitis would have higher aminotransferases. Cholestyramine can help with itching associated with cholestasis.

REFERENCE

Tong MJ, el-Farra NS, Grew MI. Clinical manifestations of hepatitis A: recent experience in a community teaching hospital. *J Infect Dis.* 1995;171 Suppl 1:S15-S18. doi:10.1093/infdis/171.supplement_1.s15

Question 30

A 27-year-old woman who takes oral contraceptives presents to clinic with mild nausea,

vomiting, and anorexia; she was recently on a cruise to the Caribbean. A comprehensive metabolic panel is obtained. Acute hepatitis panel reveals a positive hepatitis A virus (HAV) IgM. She is provided reassurance and told to rest as she recovers from HAV, and the health department is informed. Her liver tests completely normalize over the next week. She then presents 3 weeks later for routine follow-up and feels well. However, her liver tests are drawn. Ultrasound of liver does not show biliary ductal dilation. You decide to monitor liver tests weekly; however, they still have not improved after 6 weeks.

Laboratory results are below. What is the next best step in management?

- A. Conduct liver biopsy
- B. Stop oral contraceptives
- C. Perform magnetic resonance cholangiopancreatography
- D. Prescribe pentoxifylline
- E. Continue to monitor liver tests

CORRECT ANSWER: E

RATIONALE

The relapsing presentation of HAV presents with elevations of liver tests weeks after the initial presentation of symptomatic HAV and with elevated liver test results at lower levels than at initial presentation. These elevations in liver test results can last for months after initial presentation.

Laboratory Test	Result	Follow-up Result	Reference Range
Alkaline phosphatase, serum, U/L	215	204	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	1301	226	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	1058	157	10-40
Bilirubin (total), serum, mg/dL	1.2	1.1	0.3-1.0

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	232	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	2146	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	1388	10-40
Bilirubin (total), serum, mg/dL	2.1	0.3-1.0
Hepatitis A IgM	Negative	Negative

REFERENCE

Webb GW, Kelly S, Dalton HR. Hepatitis A and Hepatitis E: Clinical and Epidemiological Features, Diagnosis, Treatment, and Prevention. *Clin Microbiol Newsl.* 2020;42(21):171-179. doi:10.1016/j.clinmicnews.2020.10.001

Question 31

A 50-year-old woman presents with fatigue, nausea, and dark urine. Three months before, she had been diagnosed with acute hepatitis A and recovered completely. On examination, she has mild scleral icterus, and her abdomen is nontender and nondistended without fluid wave.

Her laboratory results are above.

What test will best identify the reason for this patient's elevated liver tests?

- A. Anti-mitochondrial antibodies
- B. Anti-smooth muscle antibodies
- C. Ceruloplasmin
- D. Ultrasound of the liver
- E. Computed tomography of abdomen with contrast

CORRECT ANSWER: B

RATIONALE

Hepatitis A virus can trigger autoimmune hepatitis, and it is important to recognize this association. Autoantibodies for autoimmune hepatitis can be elevated and should be checked, after which a liver biopsy should be obtained.

REFERENCE

Singh G, Palaniappan S, Rotimi O, Hamlin PJ. Autoimmune hepatitis triggered by hepatitis A. *Gut.* 2007;56(2):304. doi:10.1136/gut.2006.111864

Question 32

A 68-year-old man presents to the emergency department with lack of appetite (5 days) and darkening urine (1 day). He feels like his thinking has been foggy. On examination, he is arousable and conversant. He has scleral icterus, mild tenderness to palpation in the right upper quadrant with the liver edge palpable below the right costal margin, and asterixis on examination. Laboratory results are below.

What is the best next step in management?

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	245	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	5587	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	5270	10-40
Ammonia, µg/dL	125	40-70
Bilirubin (total), serum, mg/dL	3.4	0.3-1.0
Hepatitis A antibody	Positive	Negative
Hepatitis surface antigen	Negative	Negative
Hepatitis core antibody	Negative	Negative
Hepatitis C antibody	Negative	Negative
International normalized ratio	1.9	<1.1
Sodium, serum, mEq/L	132	136-145

- A. Order liver biopsy
- B. Transfer to a liver transplant center
- C. Targeted temperature management
- D. Prescribe hypertonic saline
- E. Practice extracorporeal cooling

CORRECT ANSWER: B

RATIONALE
Acute liver failure in hepatitis A, while rare, portends a poor outcome, especially in older adults. This patient should be transferred to a liver transplant center for further evaluation as soon as possible. The presence of encephalopathy and asterixis would raise concern for the progression to acute liver failure that needs urgent attention.

REFERENCE
Taylor RM, Davern T, Munoz S, et al. Fulminant hepatitis A virus infection in the United States: Incidence, prognosis, and outcomes. *Hepatology*. 2006;44(6):1589-1597. doi:10.1002/hep.21439

Question 33
A 39-year-old Asian man of Korean ethnicity presents to clinic for management of chronic hepatitis B virus. Hepatitis B surface antigen is positive, hepatitis B e antigen is positive, hepatitis E antibody is negative. His father died of hepatocellular carcinoma (HCC) at the age of 71 years.

Laboratory results are shown below.

What is the next best step with regard to HCC surveillance?

- A. Not needed as patient has immunotolerant to HBV
- B. Not indicated due to normal alpha fetoprotein
- C. Recommended due to age
- D. Indicated due to family history
- E. Indicated due to race and ethnicity

CORRECT ANSWER: D

RATIONALE
American Association for the Study of Liver Diseases guidelines recommend surveillance for HCC in patients who are Asian men older than 40 years of age. Because this patient has a family history of HCC, it would be reasonable to start HCC surveillance at this time.

REFERENCE
Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2018;68(2):723-750. doi:10.1002/hep.29913

Question 34
You are referred a 54-year-old man with a history of ulcerative colitis (UC) who was recently admitted for a flare of UC and was discharged on a short course of prednisone. You would like to start adalimumab for UC. You obtain routine laboratory testing and check his hepatitis B virus (HBV) status.

Laboratory results are listed at the top on the following page.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	105	30-120
Alpha fetoprotein, ng/mL	2.2	<10
Aminotransferase, serum alanine (ALT, SGPT), U/L	15	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	15	10-40
Bilirubin (total), serum, mg/dL	0.3	0.3-1.0

Laboratory Test	Result	Reference Range
Hepatitis core antibody	Positive	Negative
Hepatitis surface antibody	Positive	Negative
Hepatitis surface antigen	Negative	Negative
Liver Tests	Normal	Normal

What is the best next step in management?

- A. Monitor alanine aminotransferase, administer HBV DNA liver tests every 3 months
- B. Obtain ultrasound of the liver
- C. Vaccinate for HBV now
- D. Check HBV DNA now
- E. Begin entecavir treatment

CORRECT ANSWER: A

RATIONALE

This patient is at low risk overall for reactivation of HBV given his HBsAg-negative and HBcAb-positive status. However, there is still a risk that HBV reactivation could occur. As such, ALT and HBV DNA should be monitored while receiving treatment to ensure that HBV reactivation is recognized.

REFERENCES

Fidan S, Capkın E, Arica DA, Durak S, Okatan IE. Risk of hepatitis B reactivation in patients receiving anti-tumor necrosis factor- α therapy. *Int J Rheum Dis*. 2021;24(2):254-259. doi:10.1111/1756-185X.14034

Loomba R, Liang TJ. Hepatitis B Reactivation Associated With Immune Suppressive and Biological Modifier Therapies: Current Concepts, Management Strategies, and Future Directions. *Gastroenterology*. 2017;152(6):1297-1309. doi:10.1053/j.gastro.2017.02.009

Pauly MP, Tucker LY, Szpakowski JL, et al. Incidence of Hepatitis B Virus Reactivation and Hepatotoxicity in Patients Receiving Long-term Treatment With Tumor Necrosis Factor Antagonists. *Clin Gastroenterol Hepatol*. 2018;16(12):1964-1973.e1. doi:10.1016/j.cgh.2018.04.033

Question 35

A 24-year-old Indian man, who is a graduate student, presents with jaundice, nausea, and abdominal pain after recent travel to New Delhi 2 weeks before. Otherwise, he has no health problems, he has no history of alcohol use or injection drug use, and he takes no medication.

On examination, he is jaundiced and has epigastric abdominal pain without rebound or guarding.

Laboratory results are below.

What is the best next step in the evaluation of this patient's presentation?

- A. Varicella zoster polymerase chain reaction
- B. Ceruloplasmin
- C. Alpha-1 antitrypsin level
- D. Hepatitis C virus antibodies
- E. Anti-hepatitis E virus IgM

CORRECT ANSWER: E

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.1	3.5-5.5
Alkaline phosphatase, serum, U/L	278	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	4029	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	3361	10-40
Bilirubin (total), serum, mg/dL	16.5	0.3-1.0
International normalized ratio	1.2	<1.1

RATIONALE

With this patient’s travel history, hepatitis E virus should be considered in the evaluation of acute liver injury/hepatitis. Varicella zoster hepatitis typically presents with a vesicular rash. Wilson disease presents acutely with aspartate aminotransferase higher than alanine aminotransferase and a low alkaline phosphatase. Alpha-1 antitrypsin deficiency and hepatitis C virus do not typically present acutely.

REFERENCES

Chauhan A, Webb G, Ferguson J. Clinical presentations of Hepatitis E: A clinical review with representative case histories. *Clin Res Hepatol Gastroenterol*. 2019;43(6):649-657. doi:10.1016/j.clinre.2019.01.005

Wedemeyer H, Pischke S, Manns MP. Pathogenesis and treatment of hepatitis e virus infection. *Gastroenterology*. 2012;142(6):1388-1397.e1. doi:10.1053/j.gastro.2012.02.014

Question 36

A 67-year-old woman, with history of a renal transplant 1 year before, had routine labs after she returned from a trip to China. She was feeling tired and complained of mild nausea but no vomiting.

Initial laboratory studies reveal the following results shown below.

Given her history of recent travel and renal transplant, hepatitis E virus (HEV) IgM was

obtained and returned positive. Six months later, HEV IgM and HEV polymerase chain reaction (PCR) are both positive. Patient does not have any symptoms.

What do you recommend to this patient?

- A. Reassurance and supportive care
- B. Recheck HEV PCR in 3-6 months
- C. Reduce immunosuppression
- D. Treat with ribavirin
- E. Treat with interferon alpha

CORRECT ANSWER: C

RATIONALE

The initial management of chronic HEV infection in solid organ transplant recipients is reduction of immunosuppression. If, after reduction of immunosuppression, there is still detectable HEV, ribavirin is first-line treatment.

REFERENCES

Aggarwal R, Jameel S. Hepatitis E. *Hepatology*. 2011;54(6):2218-2226. doi:10.1002/hep.24674

Kamar N, Izopet J, Tripon S, et al. Ribavirin for chronic hepatitis E virus infection in transplant recipients. *N Engl J Med*. 2014;370(12):1111-1120. doi:10.1056/NEJMoa1215246

Question 37

Which patient needing hepatitis B virus (HBV) vaccination will require double-dose conventional recombinant HBV vaccine?

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	189	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	1351	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	1132	10-40
Bilirubin (total), serum, mg/dL	1.5	0.3-1.0
Hepatitis A IgM	Negative	Negative
Hepatitis C antibody	Negative	Negative
Hepatitis core antibody IgM	Negative	Negative
Hepatitis surface antigen	Negative	Negative

- A. Patient with chronic hepatitis C without cirrhosis
- B. Patient receiving methotrexate for psoriasis
- C. Patient with decompensated cirrhosis
- D. Patient receiving hemodialysis
- E. Patient receiving azathioprine for Crohn's disease

CORRECT ANSWER: D

RATIONALE

Vaccination response rates leading to immunity for patients receiving hemodialysis and those with HIV are lower with the conventional recombinant HBV vaccine. Thus, patients who are receiving hemodialysis and those with HIV who are at significant risk of acquiring HBV (due to risk exposure) should be given the high-dose vaccine.

REFERENCE

Mast EE, Weinbaum CM, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. *MMWR Recomm Rep*. 2006;55(RR-16):1-CE4.

Question 38

A 71-year-old Asian man with a history of chronic hepatitis B virus (HBV) presents to clinic to establish care for chronic HBV management. He reports that he has never received treatment in the past but also has not been engaged in medical care for his liver

disease in over 10 years. Laboratory results are shown below.

What is the next best step in the management for this patient?

- A. Begin entecavir
- B. Begin HBV vaccination series
- C. Obtain multiphase computed tomography of abdomen
- D. Obtain transient elastography
- E. Obtain transjugular liver biopsy with portal pressures

CORRECT ANSWER: D

RATIONALE

For patients who have HBV e antigen-negative, chronic HBV, if liver tests are normal and HBV DNA is lower than 2000 IU/mL, treatment is not indicated. Fibrosis assessment, either with noninvasive means or liver biopsy, is reasonable to evaluate for fibrosis and for disease activity.

REFERENCE

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 39

A 22-year-old African woman presents to clinic to establish care. She reports that her mother may have had a chronic liver disease.

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	23	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	17	10-40
Bilirubin, serum (total), mg/dL	0.6	0.3-1.0
Hepatitis B e antibody	Positive	Negative
Hepatitis B e antigen	Negative	Negative
Hepatitis B surface antigen	Positive	Negative
Hepatitis B surface antibody	Negative	Negative
Hepatitis B virus DNA, IU/mL	1350	Negative

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	30	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	25	10–40
Hepatitis B core antibody	Positive	Negative
Hepatitis B surface antibody	Negative	Negative
Hepatitis B surface antigen	Positive	Negative
Hepatitis B virus DNA, IU/mL	35,000	Negative

She is screened for hepatitis B virus (HBV). Laboratory results are shown above.

What do you recommend to her for hepatitis B management?

- A. Tenofovir disoproxil fumarate
- B. Pegylated interferon
- C. No additional intervention
- D. Percutaneous liver biopsy
- E. Multiphase computed tomography of abdomen

CORRECT ANSWER: C

RATIONALE

Treatment is not indicated in patients with immune-tolerant chronic HBV—the normal transaminases and elevated viral load. If alanine aminotransferase is elevated more than 2 times the upper limit of normal and HBV DNA is higher than 20,000 U/mL, then this patient would need to be treated.

REFERENCE

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD

2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 40

A 32-year-old woman presents to clinic for evaluation of chronic hepatitis B virus (HBV) and is currently 14 weeks pregnant with her first child. She is referred for advice on management of HBV during her pregnancy.

Laboratory results are shown below.

What is the best management plan with regards to HBV treatment?

- A. Begin entecavir now
- B. Begin tenofovir disoproxil fumarate now
- C. Begin tenofovir in the second trimester if HBV DNA is higher than 200,000 IU/mL
- D. Give hepatitis B immunoglobulin at the time of delivery to infant
- E. Perform caesarian delivery to decrease mother-to-child transmission

CORRECT ANSWER: B

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	110	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	85	10–40
Hepatitis B core antibody	Positive	Negative
Hepatitis B e antibody	Positive	Negative
Hepatitis B e antigen	Negative	Negative
Hepatitis B surface antigen	Positive	Negative
Hepatitis B surface antibody	Negative	Negative
Hepatitis B virus DNA, IU/mL	2200	Negative

RATIONALE

If a patient has an indication for HBV treatment, she should be treated whether or not she is pregnant. This patient has immune-active chronic HBV. Tenofovir disoproxil fumarate is preferred in pregnancy. The mainstay of prevention of mother-to-child transmission is HBV vaccination of the infant.

REFERENCE

Zhou K, Terrault N. Management of hepatitis B in special populations. *Best Pract Res Clin Gastroenterol.* 2017;31(3):311-320. doi:10.1016/j.bpg.2017.06.002

Question 41

A 22-year-old man with history of injection drug use and a diagnosis of chronic hepatitis B virus (HBV) infection receiving tenofovir for 3 years presents to clinic for routine follow-up. He has laboratory testing after his visit.

Laboratory results are shown below.

What do you recommend to him in clinic today?

- A. Hepatitis A virus vaccination
- B. Treatment of hepatitis C virus
- C. Fibroscan
- D. Multiphase computed tomography of liver
- E. Ultrasound liver

CORRECT ANSWER: E

RATIONALE

Patients with HBV/hepatitis D virus co-infection should receive surveillance for hepatocellular carcinoma. Patient is already immune to hepatitis A virus. Hepatitis C viremia should be confirmed with hepatitis C virus polymerase chain reaction. Multiphase computed tomography is not indicated in this patient.

REFERENCES

Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2018;68(2):723-750. doi:10.1002/hep.29913

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology.* 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 42

A 39-year-old woman with new diagnosis of chronic hepatitis B virus (HBV) presents to clinic as a referral from her obstetrician. She is currently 14 weeks pregnant and has had an uncomplicated pregnancy thus far.

Her laboratory tests were drawn at her initial prenatal visit.

The results are shown on the following page.

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	25	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	22	10-40
Cytomegalovirus IgG	Positive	Negative
Hepatitis A antibody	Positive	Negative
Hepatitis B virus DNA	Undetectable	Negative
Hepatitis C antibody	Positive	Negative
Hepatitis D antibody	Positive	Negative

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	20	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	18	10-40
Bilirubin (total), serum, mg/dL	0.2	0.3-1.0
Hepatitis core antibody	Positive	Negative
Hepatitis surface antibody	Negative	Negative
Hepatitis surface antigen	Positive	Negative

What do you recommend to her specific to her liver disease in the setting of pregnancy?

- A. Ultrasound liver
- B. HBV DNA quantitation
- C. Entecavir
- D. Bile acid quantitation
- E. Caesarian section delivery

CORRECT ANSWER: B

RATIONALE

In the second trimester, pregnant mothers should have HBV DNA tested. If maternal HBV DNA is higher than 200,000 IU/mL, antiviral therapy should be started between weeks 28 and 32 to reduce mother-to-child transmission of HBV.

REFERENCE

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Question 43

A 45-year-old man presents to clinic with a new diagnosis of hepatitis C virus (HCV) and HIV who is establishing care to discuss treatment of HCV. He uses injection drugs but quit in the past month, and he last tested negative

for HCV and HIV 2 years ago. He feels well and has no symptoms of decompensated liver disease. Before consideration of treatment for HCV, hepatitis B virus (HBV) serologies are obtained.

Laboratory results are shown below.

What should you recommend to this patient at this clinic visit?

- A. HBV DNA quantitation
- B. Ultrasound liver
- C. Tenofovir inclusive HIV treatment regimen
- D. HBV vaccination
- E. Fibroscan

CORRECT ANSWER: D

RATIONALE

This patient is at low risk of transmitting HBV to household contacts, even if HIV positive. He does not need surveillance for hepatocellular carcinoma as he does not have cirrhosis or chronic HBV. Similarly, as he does not have chronic HBV, he does not necessarily need an HBV-active HIV medication. Fibroscan would not change management. Patients with HIV or those who are immune-compromised who are hepatitis core antibody-positive should be vaccinated, as this antibody is not protective to prevent reactivation.

Laboratory Test	Result	Reference Range
Hepatitis core antibody	Positive	Negative
Hepatitis surface antibody	Negative	Negative
Hepatitis surface antigen	Negative	Negative

Laboratory Test	Result	Reference Range
Hepatitis core antibody	Positive	Negative
Hepatitis surface antibody	Negative	Negative
Hepatitis surface antigen	Negative	Negative

REFERENCE

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 44

A 78-year-old man with a remote history of injection drug use who was recently diagnosed with diffuse large B cell lymphoma is sent to you for management of hepatitis B virus (HBV). Treatment for lymphoma (R-CHOP) will begin in 2 weeks. HBV serologies were obtained: hepatitis surface antigen, negative; hepatitis core antibody, positive; hepatitis surface antibody, negative.

Laboratory results are shown above.

Which of the following is the next best step in management?

- A. Vaccinate for HBV with double-strength vaccine
- B. Check HBV DNA and liver tests every 3 months, start entecavir if HBV DNA rises 1-2 log(s)
- C. Check HBV DNA, start entecavir within 4 weeks after starting chemotherapy
- D. Start entecavir
- E. Perform ultrasound of liver

CORRECT ANSWER: D

RATIONALE

For patients who are receiving anti-CD20 therapies (eg, rituximab) and are hepatitis core antibody-positive, there is still a significant risk for reactivation of HBV. Thus, entecavir should be started ideally before or at the latest concurrently with chemotherapy.

REFERENCE

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 45

A 42-year-old Chinese woman presents for follow-up in clinic after recently completing treatment for non-Hodgkin lymphoma, a regimen that included rituximab. She has a history of immune-tolerant chronic hepatitis B virus (HBV) and was not receiving treatment before starting chemotherapy. She began HBV prophylaxis with tenofovir 2 weeks before initiation of chemotherapy. Prechemotherapy laboratory results are shown below.

What do you recommend regarding her HBV prophylaxis?

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	15	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	13	10-40
Hepatitis B core antibody	Positive	Negative
Hepatitis B surface antibody	Negative	Negative
Hepatitis B surface antigen	Positive	Negative
Hepatitis B virus DNA, IU/mL	21,000	Negative
Hepatitis B virus DNA, IU/mL	2200	Negative

- A. Discontinue tenofovir
- B. Continue tenofovir for 12 months after completion of chemotherapy
- C. Continue tenofovir indefinitely
- D. Check HBV DNA, continue tenofovir if HBV DNA is detectable for 3 months after completion of chemotherapy
- E. Continue tenofovir for 6 months after completion of chemotherapy

CORRECT ANSWER: B

RATIONALE
For patients who begin HBV prophylaxis for the reactivation of HBV in the setting of immunosuppression, HBV prophylaxis should be continued for 12 months after cessation of immunosuppressive agent(s).

REFERENCE
Loomba R, Liang TJ. Hepatitis B Reactivation Associated With Immune Suppressive and Biological Modifier Therapies: Current Concepts, Management Strategies, and Future Directions. *Gastroenterology*. 2017;152(6):1297-1309. doi:10.1053/j.gastro.2017.02.009

Question 46
A 61-year-old White man, with a history of prior immune-active chronic hepatitis B virus (HBV) receiving entecavir treatment and ulcerative colitis treated with azathioprine, presents to clinic for routine follow-up. He reports that he is in good health overall and has no complaints.

Laboratory results are shown below.

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	29	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	25	10-40
Hepatitis B virus DNA, IU/mL	2000	Negative

Three months ago, his HBV DNA was 100 IU/mL.

What is the most likely cause of this increase in HBV viral load?

- A. Hepatitis D virus superinfection
- B. Hepatitis D virus coinfection
- C. Medication noncompliance
- D. Immunosuppression-induced reactivation of HBV
- E. Viral resistance

CORRECT ANSWER: C

RATIONALE
The most likely cause of increase in HBV viral load in patients who are receiving potent preferred virologic therapies for HBV is noncompliance. Antiviral resistance is low overall for both entecavir and tenofovir.

REFERENCE
Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 47
A 71-year-old Laotian man, with history of chronic hepatitis B virus (HBV), presents with onset of abdominal distension and abdominal pain. On examination, his abdomen is protuberant without any pain elicited with palpation. Liver ultrasound with Doppler reveals a cirrhotic liver, large ascites, and patent vasculature but no liver mass.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	134	30-120
Alpha fetoprotein, ng/mL	3.2	<10
Aminotransferase, serum alanine (ALT, SGPT), U/L	18	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	20	10-40
Bilirubin (total), serum, mg/dL	1.5	0.3-1.0
Creatinine, serum, mg/dL	0.6	0.7-1.5
Hepatitis B e antibody	Positive	Negative
Hepatitis B e antigen	Negative	Negative
Hepatitis B surface antigen	Positive	Negative
Hepatitis B virus DNA, IU/mL	980	Negative

Laboratory results are shown above.

What do you recommend at this time?

- A. Entecavir
- B. Ciprofloxacin for prophylaxis
- C. Ceftriaxone
- D. Fluid restriction
- E. Multiphase liver magnetic resonance imaging

CORRECT ANSWER: A

RATIONALE

Patients with decompensated cirrhosis and chronic HBV should be treated regardless of HBV DNA level. There is no indication for antibiotics. Magnetic resonance imaging of the abdomen with large ascites will be low yield for imaging the liver.

REFERENCE

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 48

A 45-year-old Egyptian man, with a prior history of chronic hepatitis B as a result of vertical transmission, presents to clinic after being lost to follow-up for several years. He feels well and has been in good health since he was last seen in clinic. Laboratory results are shown below.

What do you recommend for management?

- A. Liver ultrasound
- B. Multiphase computed tomography of liver
- C. Repeat hepatitis B surface antigen
- D. Entecavir
- E. Hepatitis C antibodies

CORRECT ANSWER: A

RATIONALE

Very rarely, patients can have spontaneous hepatitis B surface antigen loss. If a patient has cirrhosis, family history of hepatocellular carcinoma, or long duration of infection, hepatocellular carcinoma surveillance is recommended.

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	28	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	30	10-40
Hepatitis B core antibody	Positive	Negative
Hepatitis B surface antibody	Positive	Negative
Hepatitis B surface antigen	Negative	Negative

REFERENCE

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 49

A 53-year-old woman, with a history of chronic hepatitis B virus (HBV) receiving entecavir and type 2 diabetes mellitus taking insulin, is referred for evaluation of chronic HBV and elevated liver test results. She has no symptoms at present, and her examination is unremarkable. Liver ultrasound does not show any liver masses. Laboratory results are shown below.

What is your next step in managing this patient?

- A. Transient elastography with controlled attenuation parameter
- B. Assessment for HBV viral resistance
- C. Addition of tenofovir
- D. Multiphase computed tomography of liver
- E. Abbreviated magnetic resonance imaging

CORRECT ANSWER: A

RATIONALE

In patients with HBV and low HBV DNA levels but elevated liver test results, other etiologies of liver disease should be entertained. In this patient with risk factors for nonalcoholic fatty liver disease, nonalcoholic steatohepatitis could be a possible etiology for liver test result elevations.

REFERENCE

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 50

A healthy 21-year-old man presents to clinic with a concern about liver disease. He is sexually active with men and women currently and was using injection drugs 2 years ago. Given this history, laboratory studies were obtained.

Hepatitis B surface antigen is positive, and hepatitis C antibody and HIV antibody are negative. Otherwise, he has normal liver tests.

What other testing is indicated at this time?

- A. Anti-smooth muscle antibody
- B. Hepatitis C virus RNA polymerase chain reaction
- C. Hepatitis D virus RNA polymerase chain reaction
- D. Hepatitis D virus antibody
- E. Hepatitis E virus antibody

CORRECT ANSWER: D

RATIONALE

Patients with risk factors for hepatitis D virus infection should be screened including persons from areas of endemicity, those with HIV, and those who have a history of injection drug use. The initial screening test is the hepatitis D virus antibody test.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	161	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	58	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	46	10-40
Bilirubin, serum (total), mg/dL	0.8	0.3-1.0
Hepatitis B virus DNA, IU/mL	200	Negative

REFERENCE

Koh C, Heller T, Glenn JS. Pathogenesis of and New Therapies for Hepatitis D. *Gastroenterology*. 2019;156(2):461-476.e1. doi:10.1053/j.gastro.2018.09.058

CHAPTER 6

Metabolic, hereditary, inflammatory and vascular diseases of the liver

Mike Kriss, MD and Jonathan Stine, MD

Question 1

A 54-year-old woman with a past medical history of type 2 diabetes, hypertension, and hyperlipidemia is referred to you for evaluation of unexplained elevated liver-associated enzymes over the previous year. Laboratory tests reveal a complete blood count and the following additional results shown below.

Ultrasound of the liver reveals an enlarged and echogenic liver with patent portal and hepatic veins, and no radiographic signs of portal hypertension or cirrhosis. You discuss proceeding with liver biopsy for diagnostic purposes.

Which of the following is the most likely histologic finding?

- A. 2+ iron in the hepatocytes, steatosis, interface hepatitis
- B. Hepatocyte ballooning, lobular inflammation, steatosis
- C. Interface hepatitis, plasma cells, steatosis

- D. Portal lymphocytic infiltrate, steatosis, endotheliitis

CORRECT ANSWER: B**RATIONALE**

This patient is expected to have nonalcoholic steatohepatitis (NASH) based on her history of uncontrolled metabolic syndrome, imaging suggesting hepatic steatosis and her negative testing for viral hepatitis. The definitive diagnosis of NASH remains a histologic diagnosis. The key histologic features for a diagnosis of NASH include hepatic steatosis, lobular inflammation, and ballooned hepatocytes. Collectively, these 3 histologic findings make up the NAFLD Activity Score. Endotheliitis is a hallmark of acute cellular rejection in liver transplant recipients. Although iron can be found in liver tissue in patients with NASH, it is not required nor characteristic of this diagnosis. Interface hepatitis is most commonly seen in patients with autoimmune liver disease.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.5	3.5-5.5
Aminotransferase, serum alanine (ALT, SGPT), U/L	63	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	57	10-40
Ferritin, serum, ng/mL	550	24-307
Hemoglobin A1C, %	8.3%	4.0-5.6
Hepatitis B surface antigen	Negative	Negative
Hepatitis B surface antibodies	Positive	Negative
Hepatitis B core antibodies (total)	Negative	Negative
Hepatitis C virus antibodies	Negative	Negative

REFERENCES

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Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;67(1):328-357. doi:10.1002/hep.29367

Kleiner DE, Brunt EM, van Natta M, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology*. 2005;41(6):1313-1321. doi:10.1002/hep.20701

Question 2

A 55-year-old woman is referred to your clinic for further diagnosis and management of long-standing history of elevated liver enzymes: alanine aminotransferase, 67 U/L (reference range, 10-40 U/L) and aspartate aminotransferase, 43 U/L (reference range, 10-40 U/L). An extensive serologic workup was negative, and imaging was notable for an echogenic and enlarged liver. The patient does not have a history of alcohol use. You suspect nonalcoholic steatohepatitis (NASH) and order percutaneous liver biopsy, which confirms the diagnosis of NASH and demonstrates stage 2 fibrosis.

Which of the following statements would be the best strategy for the management of this patient?

- A. Iron depletion through phlebotomy
- B. Lifestyle modification with dietary changes
- C. Initiate metformin therapy
- D. Initiate Vitamin E therapy

CORRECT ANSWER: B

RATIONALE

At this point in time, there is no regulatory agency-approved drug therapy for NASH, based largely on a lack of efficacy. Current off-label options that can be considered are vitamin E or pioglitazone, based on data from the PIVENS Trial, or obeticholic acid (OCA) based on data from the FLINT Trial. The PIVENS Trial enrolled 247 adults with NASH and without diabetes and randomized patients to pioglitazone, vitamin E, or placebo for 96 weeks. Vitamin E at a dose of 800 IU/d was superior to placebo as it led to significantly greater rate of histologic improvement in NASH activity (43% vs 19%, $P < .01$). Pioglitazone had greater rates of histologic improvement in NASH activity as well when compared with placebo (34% vs. 19%, $P = .04$); however, this rate was not as significant. Importantly, neither vitamin E nor pioglitazone led to improvement in liver fibrosis stage. The FLINT Trial enrolled 283 adults and randomized them to receive either OCA or placebo for 72 weeks. Forty-five percent of patients receiving OCA achieved histologic improvement in NASH (at least a 2-point improvement in NAFLD Activity Score without fibrosis stage worsening) compared with 21% in the placebo group (relative risk, 2.2; 95% confidence interval, 1.4-3.3, $P < .01$). Importantly, 35% of patients receiving OCA had at least a 1-point improvement in liver fibrosis stage compared with 19% of those receiving placebo ($P = .04$). Although drug therapy should be considered only for patients with NASH, lifestyle modification should be recommended for patients with all types of nonalcoholic fatty liver disease, including NASH, which is the progressive type of nonalcoholic fatty liver disease. Neither metformin nor phlebotomy have been shown to improve liver histology.

REFERENCES

Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;67(1):328-357. doi:10.1002/hep.29367

Younossi ZM, Corey KE, Lim JK. AGA Clinical Practice Update on Lifestyle Modification Using Diet and Exercise to Achieve Weight Loss in the Management of Nonalcoholic Fatty Liver Disease: Expert Review. *Gastroenterology*. 2021;160(3):912-918. doi:10.1053/j.gastro.2020.11.051

Question 3

You have been seeing a 65-year-old man with biopsy-proven nonalcoholic steatohepatitis (NASH) and stage 3 liver fibrosis for the past 3 years. At his follow-up appointment, he is inquiring about his long-term prognosis.

Which of the following is the leading cause of long-term mortality in patients like the one presented?

- A. Cardiovascular disease
- B. Hepatocellular carcinoma
- C. Infection
- D. Lung cancer

CORRECT ANSWER: A

RATIONALE

Patients with nonalcoholic fatty liver disease (NAFLD) and NASH have increased morbidity and mortality when compared with the general population. Cardiovascular disease is a leading cause of long-term mortality in patients with NAFLD and NASH. Although extrahepatic cancers—including breast, colorectal, prostate, gastric, esophageal, renal, and ovarian—are also leading causes of long-term mortality, primary lung cancer is not associated with NAFLD or NASH. Although hepatocellular carcinoma occurs more frequently in patients with NAFLD and NASH, both with and without cirrhosis, it occurs less frequently than cardiovascular disease or extrahepatic cancer.

REFERENCES

Allen AM, Hicks SB, Mara KC, Larson JJ, Therneau TM. The risk of incident extrahepatic can-

cers is higher in non-alcoholic fatty liver disease than obesity - A longitudinal cohort study. *J Hepatol*. 2019;71(6):1229-1236. doi:10.1016/j.jhep.2019.08.018

Simon TG, Roelstraete B, Khalili H, Hagström H, Ludvigsson JF. Mortality in biopsy-confirmed nonalcoholic fatty liver disease: results from a nationwide cohort. *Gut*. 2021;70(7):1375-1382. doi:10.1136/gutjnl-2020-322786

Stine JG, Wentworth BJ, Zimmet A, et al. Systematic review with meta-analysis: risk of hepatocellular carcinoma in non-alcoholic steatohepatitis without cirrhosis compared to other liver diseases. *Aliment Pharmacol Ther*. 2018;48(7):696-703. doi:10.1111/apt.14937

Question 4

A 53-year-old woman with metabolic syndrome has a history of biopsy-proven nonalcoholic steatohepatitis with stage 1 liver fibrosis. Beyond traditional metabolic risk factors, such as diabetes or obesity, which of the following conditions are associated with an increased risk for nonalcoholic fatty liver disease (NAFLD)?

- A. B-cell lymphoma
- B. Lung cancer
- C. Pseudogout
- D. Psoriasis

CORRECT ANSWER: D

RATIONALE

There are multiple reported extrahepatic associations between NAFLD and psoriasis. Psoriasis may be associated with greater rates of fibrosis progression. Other important extrahepatic associations have been described between NAFLD and cardiovascular disease, chronic kidney disease, obstructive sleep apnea, osteoporosis, iron overload, venous thromboembolism, and various endocrinopathies (eg, type 2 diabetes, thyroid disease, polycystic ovary syndrome). Extrahepatic cancers

are common in NAFLD as well, however, lung cancer is not one of them. Pseudogout is associated with hereditary hemochromatosis and B-cell lymphoma is associated with chronic hepatitis C infection.

REFERENCES

Allen AM, Hicks SB, Mara KC, Larson JJ, Therneau TM. The risk of incident extrahepatic cancers is higher in non-alcoholic fatty liver disease than obesity - A longitudinal cohort study. *J Hepatol*. 2019;71(6):1229-1236. doi:10.1016/j.jhep.2019.08.018

Li AA, Ahmed A, Kim D. Extrahepatic Manifestations of Nonalcoholic Fatty Liver Disease. *Gut Liver*. 2020;14(2):168-178. doi:10.5009/gnl19069

VanWagner LB, Rinella ME. Extrahepatic Manifestations of Nonalcoholic Fatty Liver Disease. *Cur Hepatol Rep*. 2016;15(2):75-85. doi:10.1007/s11901-016-0295-9

Question 5

A 55-year-old man recently underwent liver biopsy to stage his nonalcoholic steatohepatitis (NASH). Histologic analysis according to NASH Clinical Research Network Criteria shows a NAFLD Activity Score of 5. Liver fibrosis stage is assessed as stage 2. In addition to enacting lifestyle modification with dietary change and increased physical activity, he enrolls in a phase II drug trial, which requires he undergo serial disease assessment with biomarkers.

Which of the following assessments did he most likely undergo for this trial?

- A. Controlled attenuation parameter
- B. Cytokeratin-18
- C. Enhanced liver fibrosis test
- D. Magnetic resonance imaging proton density fat fraction

CORRECT ANSWER: D

RATIONALE

Although all of the choices are biomarkers that may be used to monitor for disease activity in patients with NASH, magnetic resonance imaging proton density fat fraction (MRI-PDFF) is the most accurate and sensitive biomarker to assess changes in liver fat content. MRI-PDFF is a noninvasive method developed to quantify liver fat. MRI-PDFF has the highest diagnostic accuracy compared with other noninvasive assessment methods. This is why MRI-PDFF is being used more commonly as the primary end point in early phase II NASH drug trials.

REFERENCES

Loomba R, Guy C, Bashir M, Harrison S, BP. Magnetic resonance imaging proton density fat fraction (MRI-PDFF) to predict treatment response on NASH liver biopsy: a secondary analysis of the resmetirom randomized placebo controlled Phase 2 clinical trial. *EASL International Liver Congress*. Published online 2020.

Noureddin M, Lam J, Peterson M, et al. Utility of magnetic resonance imaging versus histology for quantifying changes in liver fat in non-alcoholic fatty liver disease trials. *Hepatology*. 2013;58(6):1930-1940. <https://www.cochranelibrary.com/central/doi/10.1002/central/CN-00911582/full>

Stine JG, Munaganuru N, Barnard A, et al. Change in MRI-PDFF and Histologic Response in Patients with Nonalcoholic Steatohepatitis: A Systematic Review and Meta-Analysis. *Clin Gastroenterol Hepatol*. Published online 2020. doi:10.1016/j.cgh.2020.08.061

Question 6

A 60-year-old woman with nonalcoholic steatohepatitis has just decided to begin an exercise program. She leads a sedentary lifestyle and gets fewer than 90 minutes each week of physical activity. Her body mass index is 35 kg/m². She also has hyperlipidemia, hypertension, and diabetes. Her

most recent blood pressure was 145/90 mmHg, and her last fasting bloodwork showed a blood glucose of 150 mg/dL (reference range, 70-99 mg/dL) and a high-density lipoprotein of 35 mg/dL (reference range, <30 mg/dL). She was recently prescribed pioglitazone to treat her NASH. Her treating clinician told her that she needs to lose weight over the next 3 to 6 months in addition to starting drug therapy for her fatty liver disease.

Which of the following exercise regimens would you recommend for this patient?

- A. 150-300 minutes of moderate-intensity exercise weekly
- B. 150-300 minutes of vigorous-intensity exercise weekly
- C. 75-150 minutes of moderate-intensity exercise weekly
- D. 75-300 minutes of vigorous-intensity exercise weekly

CORRECT ANSWER A

RATIONALE

Lifestyle modification with dietary change and increased physical activity should be recommended for all patients with NAFLD, regardless of their disease stage. Current consensus guidelines from the American Gastroenterological Association (AGA) recommend either 150 to 300 minutes weekly of moderate-intensity aerobic exercise, such as walking, or 75 to 150 minutes weekly of vigorous-intensity exercise, such as jogging or cycling. The AGA suggests that this aerobic exercise be paired with resistance training. When combined with dietary change that includes avoiding fructose-rich beverages, limiting red meat, and following a Mediterranean-based diet, this amount of physical activity can be a vehicle for the modest amount of weight loss recommended to improve liver histology and metabolic disease in patients with NAFLD.

REFERENCES

Thorp A, Stine JG. Exercise as Medicine: The

Impact of Exercise Training on Nonalcoholic Fatty Liver Disease. *Cur Hepatol Rep*. Published online 2020. doi:10.1007/s11901-020-00543-9

Younossi ZM, Corey KE, Lim JK. AGA Clinical Practice Update on Lifestyle Modification Using Diet and Exercise to Achieve Weight Loss in the Management of Nonalcoholic Fatty Liver Disease: Expert Review. *Gastroenterology*. 2021;160(3):912-918. doi:10.1053/j.gastro.2020.11.051

Question 7

A 60-year-old woman with biopsy-proven nonalcoholic steatohepatitis (NASH) and stage 2 liver fibrosis has been struggling to lose weight for several years despite adherence to lifestyle modification, including attending regular 60-minute moderate-intensity water aerobics classes 3 days a week and meeting regularly with a dietitian, and pharmacologic therapy with vitamin E. Her medical history is notable for hypertension treated with amlodipine, hyperlipidemia for which she takes a statin, and obstructive sleep apnea that is well controlled with her continuous positive airway pressure machine. Although her osteoarthritis in both knees limits her ability to perform regular exercise, she has no active cardiopulmonary symptoms. Her current body mass index is 43 kg/m² and her blood pressure is 120/80 mmHg. Her fasting lipid panel shows low-density lipoprotein of 70 mg/dL (reference range, <100 mg/dL) and total cholesterol of 130 mg/dL (reference range, <200).

What is the next most appropriate step in her clinical management to improve her NASH?

- A. Prescribe semaglutide in addition to vitamin E
- B. Refer her for a bariatric surgery evaluation
- C. Refer her for orthopedic surgery for bilateral knee replacement
- D. Substitute pioglitazone for vitamin E

CORRECT ANSWER: B

RATIONALE

In the absence of surgical contraindications, bariatric surgery is indicated in patients with NASH who have class III obesity and are unable to lose weight. Long-term outcomes of bariatric surgery show that at 5 years, many patients will lose enough weight to resolve their NASH without fibrosis stage worsening. In this patient, she has failed to lose weight or improve her NASH with standard lifestyle modification and drug therapy. Substituting pioglitazone would not be expected to lead to weight loss and in fact may lead to weight gain should she develop lower extremity edema, a known side effect. Bilateral knee replacement may help her functional status; however, she is already achieving recommended amounts of physical activity and still has not lost weight. Although semaglutide was recently approved by the US Food and Drug Administration (FDA) as a weight loss drug, its efficacy in NASH remains under evaluation.

REFERENCES

Lassailly G, Caiazzo R, Ntandja-Wandji LC, et al. Bariatric Surgery Provides Long-term Resolution of Nonalcoholic Steatohepatitis and Regression of Fibrosis. *Gastroenterology*. 2020;159(4):1290-1301.e5. doi:10.1053/j.gastro.2020.06.006

Wilding JPH, Batterham RL, Calanna S, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. *N Engl J Med*. 2021;384(11):989. doi:10.1056/NEJMoa2032183

Question 8

An otherwise healthy 28-year-old man is referred

to you for evaluation after blood work obtained as a part of a routine life insurance examination found an elevated total bilirubin level. He has no medical problems and takes no medications, either over the counter or prescribed, and no herbal supplements. His physical examination is normal.

You repeat his laboratory testing and find the following results shown below.

Which of the following statements most accurately describes this patient’?

- A. Genetic testing would show variation in the *ABCB11* gene
- B. Genetic testing would show variation in the *ATP7B* gene
- C. Increased risk for alcohol toxicity
- D. Periods of fasting or stress may increase his serum bilirubin level

CORRECT ANSWER: D

RATIONALE

This healthy young man has a mild indirect hyperbilirubinemia in the setting of normal liver function and normal hematocrit. He most likely has Gilbert’s syndrome, and no further evaluation or treatment is needed. Recognition of the disorder and discussion of the mode of inheritance is more important to avoid unnecessary testing in the patient and family members. This is a benign disorder that is due to genetic variations in the *UGT1A1* gene that results in decreased activity of the bilirubin uridine diphosphate glucuronosyltransferase enzyme. Gilbert’s syndrome is not

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	4.5	3.5-5.5
Alkaline phosphatase, serum, U/L	98	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	23	10-40
Bilirubin, serum Total, mg/dL Direct, mg/dL	1.8 0.5	0.3-1.0 0.1-0.3
Aminotransferase, serum aspartate (AST, SGOT), U/L	18	10-40
Hematocrit, blood, %	45	42-50
International normalized ratio	1.0	<1.1
Platelet count, plts/ μ L	350,000	150,000-450,000

associated with risk for progressive liver disease nor is it associated with an increased risk for alcohol toxicity. Periods of fasting or stress may lead to an increase in his serum bilirubin, albeit this is typically not seen with a level of more than 4.0 g/dL. In rare instances, Gilbert's syndrome can lead to a mild hemolytic anemia. Mutations in the *ATP7B* gene are associated with Wilson's disease. The *ABCB11* gene controls bile salt export. Mutations in this gene can be associated with benign recurrent intrahepatic cholestasis, progressive familial intrahepatic cholestasis, and intrahepatic cholestasis of pregnancy.

REFERENCE

Erlinger S, Arias IM, Dhumeaux D. Inherited disorders of bilirubin transport and conjugation: new insights into molecular mechanisms and consequences. *Gastroenterology*. 2014;146(7):1625-1638. doi:10.1053/j.gastro.2014.03.047

Question 9

A 20-year-old man presents to your clinic for elevated liver function testing. He reports having abdominal pain 2 weeks ago, but it self-resolved and he currently feels well. You review the following laboratory testing results shown below.

What is this patient's most likely diagnosis?

- A. Crigler-Najjar type 1
- B. Cholestatic relapsing hepatitis A viral infection
- C. Dubin-Johnson syndrome
- D. Rotor syndrome

CORRECT ANSWER: A

RATIONALE

Crigler-Najjar is an autosomal recessive disorder resulting in mutations in the *UGT1A1* gene leading to loss of function in bilirubin glucuronidation. Crigler-Najjar is characterized clinically by marked increases in unconjugated bilirubin levels from birth, putting an infant at risk for kernicterus. There are 2 types of Crigler-Najjar, Type 1 and Type 2. Type 1 is characterized by the complete absence of the functional enzyme, resulting in the most severe phenotype of the disorder. Crigler-Najjar, type 1 is often fatal if untreated. Crigler-Najjar, type 2 is the milder variant with reduced (<20% of people have normal function), but not absent, enzyme activity. Rotor syndrome and Dubin-Johnson syndrome cause elevations in conjugated bilirubin levels. Dubin-Johnson syndrome is due to a genetic variation in the *ABCC2* gene, resulting in a defect in the canalicular transport of conjugated bilirubin into the bile. The liver appears black on gross examination due to the defects in canalicular transport. Liver enzymes and serum bile acid levels are normal and individuals with Dubin-Johnson syndrome do not develop liver failure. Cholestatic relapsing hepatitis A viral infection usually presents in fewer than 5% of patients with known acute hepatitis A infection. The presentation is usually characterized by marked jaundice, pruritus, fever, weight loss, diarrhea, and malaise.

REFERENCE

Erlinger S, Arias IM, Dhumeaux D. Inherited disorders of bilirubin transport and conjugation: new insights into molecular mechanisms and consequences. *Gastroenterology*. 2014;146(7):1625-1638. doi:10.1053/j.gastro.2014.03.047

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	4.1	3.5-5.5
Alkaline phosphatase, serum, U/L	105	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	21	10-40
Bilirubin, serum Total, mg/dL Direct, mg/dL	3.8 3.5	0.3-1.0 0.1-0.3
Aminotransferase, serum aspartate (AST, SGOT), U/L	22	10-40
International normalized ratio	1.0	<1.1
Platelet count, plts/ μ L	280,000	150,000-450,000

Laboratory Test	Result	Reference Range
Antimitochondrial antibody, titer	1:128	≤1:5
Cholesterol, serum, Total, mg/dL	300	<200
IgM serum, mg/dL	350	45-150
Vitamin D metabolites, serum, ng/mL	20	30-60

Question 10

A 45-year-old woman is referred to you for further management of an elevated alkaline phosphatase level of 450 U/L in the setting of chronic fatigue. Her past medical history is significant for both hyperlipidemia as well as hypothyroidism. Her body mass index is 24 kg/m², and her examination is normal. Other pertinent laboratories show the following results shown above.

Which of the following complications is she at increased risk for due to her liver disease?

- A. Cardiovascular events
- B. Gastroesophageal varices
- C. Systemic lupus
- D. Osteoarthritis

CORRECT ANSWER: B

RATIONALE

This patient has primary biliary cholangitis (PBC) as indicated by her elevated alkaline phosphatase, positive antimitochondrial antibody, and elevated IgM in addition to being female and in her forties. PBC can be associated with the development of pre-sinusoidal portal hypertension in the absence of cirrhosis, resulting in risk for developing varices. The Mayo PBC Risk Index can be calculated to determine who is at risk for pre-sinusoidal portal hypertension with a score higher than 4.1 indicating a screening esophagogastroduodenoscopy is reasonable to pursue. PBC increases the risk for low bone density, and routine dual-energy x-ray

absorptiometry scans should be obtained every 2 to 3 years. Fatigue is found in up to 70% of patients with PBC but does not improve with treatment. Hyperlipidemia is directly related to PBC but does not lead to an increased risk of premature cardiovascular disease events in the absence of other traditional cardiovascular disease risk factors. Patients are at increased risk of Sjogren’s syndrome, thyroid disease, scleroderma, and rheumatoid arthritis. There is no known increased risk of osteoarthritis or systemic lupus in PBC.

REFERENCE

Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2019;69(1):394-419. doi:10.1002/hep.30145

Question 11

A 48-year-old woman is referred for further diagnosis and management with the following laboratory test results shown below.

Which of the following would most likely follow with a favorable prognosis in this patient?

- A. Statin therapy
- B. Reduction in alkaline phosphatase
- C. Vitamin K therapy
- D. Female gender

CORRECT ANSWER: B

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	400	30-120
Antimitochondrial antibody, titer	1:1280	≤1:5
Bilirubin (total), serum, mg/dL	1.9	0.3-1.0
Hematocrit, blood, %	28	37-47
International normalized ratio	1.4	<1.1
Platelet count, plts/μL	210,000	150,000-450,000

RATIONALE

Several clinical and biochemical features have prognostic value in PBC. Patients who have a response to medical therapy, defined as a 40% reduction or less than 1.67 times the upper limit of normal in alkaline phosphatase after 12 months of treatment, have a favorable course and typically do not progress to end-stage liver disease. PBC tends to be a more slowly progressive chronic liver disease compared with other chronic liver disease etiologies. Patients with AMA-negative PBC have a similar natural history as patients with AMA-positive PBC. PBC is much more common in women than men, but there is no difference in prognosis. While PBC patients may suffer from hypercholesterolemia, there is no increased risk of cardiovascular events. Finally, while some fat-soluble vitamins might be malabsorbed, there is no increased risk in the noncirrhosis patient.

REFERENCE

Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2019;69(1):394-419. doi:10.1002/hep.30145

Question 12

A 42-year-old woman is recently diagnosed with primary biliary cholangitis (PBC). Transient elastography shows stage 1 fibrosis.

Her laboratory test results demonstrate the following shown below.

During her clinic visit, you discuss initiating treatment with first-line therapy. Which of the following will be reduced with the initiation of therapy in this patient's case?

- A. Symptoms of pruritus
- B. Level of serum high-density lipoprotein
- C. Risk of bleeding from gastroesophageal varices
- D. Risk of osteopenia and osteoporosis

CORRECT ANSWER: C

RATIONALE

Ursodeoxycholic acid (UDCA) as a first-line drug treatment for patients with PBC has many ascribed benefits including reducing the risk of the development of gastroesophageal varices. UDCA is also associated with a reduction in serum low-density lipoprotein and slower histologic progression; however, it does not improve associated autoimmune features, bone disease, fatigue, or pruritus.

REFERENCE

Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2019;69(1):394-419. doi:10.1002/hep.30145

Question 13

A 50-year-old woman was found to have an elevated alkaline phosphatase level to 400 U/L (reference range, 30-120 U/L) on routine laboratory tests obtained at her annual health wellness examination. She is otherwise healthy, although she does disclose a family history of lupus and Crohn's ileocolitis. Her body mass index is 24 kg/m², and her examination does not show any stigmata of chronic liver disease. Other pertinent laboratory test results include antinuclear antibodies (ANA) with 1:1280 titer (reference range, ≤1:40), antimitochondrial antibodies (AMA) with 1:640 titer (reference range, ≤1:5).

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	250	30-120
Antimitochondrial antibody, titer	1:1280	≤1:5
Bilirubin (total), serum, mg/dL	1.5	0.3-1.0
IgM serum, mg/dL	230	45-150

Which of the following autoimmune diseases is associated with this patient's diagnosis?

- A. Addison's disease
- B. Systemic lupus
- C. Multiple sclerosis
- D. Sjogren's syndrome

CORRECT ANSWER: D

RATIONALE

This patient has primary biliary cholangitis (PBC). Three major autoimmune diseases have been shown to occur significantly more often in PBC including: 1) Sjogren's syndrome; 2) CREST (calcinosis, Raynaud's, esophageal dysfunction, sclerodactyly, and telangiectasias) or scleroderma (systemic sclerosis); 3) Raynaud's disease. Routine history taking in the clinic should screen patients for the development of these common extrahepatic autoimmune diseases. The association between autoimmune thyroid disease and celiac disease have also been described; however, the evidence supporting this is less robust at this time. There is no known increased risk of Addison's disease, systemic lupus, or multiple sclerosis.

REFERENCES

Floreani A, Franceschet I, Cazzagon N, et al. Extrahepatic autoimmune conditions associated with primary biliary cirrhosis. *Clin Rev Allergy Immunol.* 2015;48(2-3):192-197. doi:10.1007/s12016-014-8427-x

Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. *Hepatology.* 2019;69(1):394-419. doi:10.1002/hep.30145

Question 14

A 29-year-old man is referred to you for further diagnosis and management of an elevated alkaline phosphatase level of 499 U/L (reference

range, 30-120 U/L) and total bilirubin level of 1.0 mg/dL (reference range, 0.3-1.0 mg/dL).

His past medical history is notable for ulcerative colitis for which he is maintained on infliximab, but no previous history of liver disease. Magnetic resonance cholangiopancreatography reveals multiple strictures and dilations in his intrahepatic and extrahepatic biliary ducts.

Which of the following primary malignancies is of most concern in this patient?

- A. Gallbladder cancer
- B. Mucinous cystadenoma
- C. Hepatocellular carcinoma
- D. Ampullary carcinoma

CORRECT ANSWER: A

RATIONALE

Patients with PSC are at increased risk for primary gallbladder carcinoma, and surveillance imaging should be done annually to detect mass lesions in the gallbladder. In patients who are found to have a gallbladder mass lesion, cholecystectomy should be pursued, regardless of the size, if underlying liver disease permits. Patients for PSC are also at increased risk for cholangiocarcinoma and although the optimal screening and surveillance testing remains somewhat controversial, contrasted magnetic resonance imaging every 12 months with or without tumor markers (eg, CA 19-9, carcinoembryonic antigen) can be considered. Patients with PSC do not appear to have an increased risk of hepatocellular carcinoma in the absence of cirrhosis, although mixed hepatocellular carcinoma-cholangiocarcinoma tumors have been reported. They are also not at increased risk of mucinous cystadenoma or ampullary carcinoma.

REFERENCE

Chapman R, Fevery J, Kalloo A, et al. Diagnosis and management of primary sclerosing cholangitis. *Hepatology.* 2010;51(2):660-678. doi:10.1002/hep.23294

Question 15

A 24-year-old man with newly diagnosed primary sclerosing cholangitis (PSC) presents for initial consultation. His past medical history is unremarkable. He feels well and has no specific complaints. His aspartate aminotransferase, alanine aminotransferase, total bilirubin, albumin, international normalized ratio, and platelet count are all normal. His alkaline phosphatase is elevated to 347 U/L (reference range, 30-120 U/L). Magnetic resonance cholangiopancreatography does not show any extrahepatic biliary dilation, but his intrahepatic ducts are dilated in the secondary and tertiary radicles.

Which of the following do you recommend for further management of this patient?

- A. Colonoscopy
- B. Endoscopic retrograde cholangiopancreatography with sphincterotomy and stenting
- C. Liver biopsy
- D. Ursodeoxycholic acid at 30 mg daily

CORRECT ANSWER: A

RATIONALE

Because PSC is strongly associated with inflammatory bowel disease (IBD), a full colonoscopy with biopsies should be performed in all patients with a new diagnosis of PSC and no previous history of symptoms of IBD. Moreover, if a diagnosis of IBD is made, surveillance colonoscopy with biopsies should be performed every 1 to 2 years from the time of PSC diagnosis given the increased risk of colorectal cancer. Liver biopsy is rarely clinically useful in patients with PSC as the biopsy can be made based on laboratory testing and imaging in most cases. ERCP

with sphincterotomy and stenting is unlikely to be of use in small-duct PSC. Ursodeoxycholic acid does not impact the natural history of PSC. Moreover, it can be harmful in higher doses (28-30 mg daily) and is not recommended in the treatment of PSC, even for the chemoprevention of colorectal cancer in patients with PSC and IBD.

REFERENCE

Chapman R, Fevery J, Kalloo A, et al. Diagnosis and management of primary sclerosing cholangitis. *Hepatology*. 2010;51(2):660-678. doi:10.1002/hep.23294

Question 16

A 29-year-old man with cirrhosis secondary to primary sclerosing cholangitis (PSC) has had several episodes of bacterial cholangitis over the previous year requiring hospitalization and intensive care unit-level care. Accordingly, he is listed for liver transplantation. Over the past 3 weeks, he has developed worsening jaundice and new onset of ascites. Vital signs are notable for temperature of 37°C, blood pressure of 120/80 mmHg, and heart rate of 80 bpm. On examination, he is alert, oriented with scleral icterus and mild temporal wasting. He has a positive fluid wave and shifting dullness. Laboratory test results are notable for the following shown below.

What is the most likely reason for his clinical deterioration?

- A. Cholangiocarcinoma
- B. Drug-induced liver injury
- C. Portal vein thrombosis
- D. Recurrent cholangitis

Laboratory Test	Result 1 Month Ago	Result Today	Reference Range
Alkaline phosphatase, serum, U/L	250	867	30-120
Bilirubin (total), serum, mg/dL	2.1	14.1	0.3-1.0
Carbohydrate antigen 19-9 (CA 19-9), serum, U/mL	--	250	0-37

CORRECT ANSWER: A

RATIONALE

Patients with PSC are at increased risk for developing cholangiocarcinoma (CCA) with a 10-year cumulative incidence of about 10%. Given the risk of CCA in patients with PSC, it is recommended that an evaluation for CCA should be performed in all patients with deterioration of their performance status or liver biochemical-related parameters. This can be pursued largely with contrasted cross-sectional imaging with magnetic resonance cholangiopancreatography and tumor markers, including CA 19-9 and carcinoembryonic antigen. Importantly, tumor markers can be falsely elevated in the setting of hyperbilirubinemia; therefore, elevations cannot be interpreted with confidence in this setting. Recurrent cholangitis is unlikely in the absence of fevers and though portal vein thrombosis may occur more commonly in patients with PSC, CCA remains the most likely diagnosis.

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Chapman R, Fevery J, Kalloo A, et al. Diagnosis and management of primary sclerosing cholangitis. *Hepatology*. 2010;51(2):660-678. doi:10.1002/hep.23294

Lindor KD, Kowdley K v, Harrison ME. ACG Clinical Guideline: Primary Sclerosing Cholangitis. *Am J Gastroenterol*. 2015;110(5):646-659; quiz 660. doi:10.1038/ajg.2015.112

Question 17

A 60-year-old man is referred to your clinic for further diagnosis and management of progressive jaundice of unclear etiology that developed over the previous month. He mentions non-bloody loose stools that occur once per week.

Current laboratory test results are shown below.

Cross-sectional imaging with magnetic resonance cholangiopancreatography demonstrates fullness in the pancreatic head and dilated intra- and extrahepatic bile ducts.

Which of the following is the best next step of management for this patient?

- A. Initiate corticosteroids
- B. Colonoscopy
- C. Endoscopic retrograde cholangiopancreatography
- D. Referral to surgery

CORRECT ANSWER: A

RATIONALE

This patient has IgG4-related disease (IgG4-RD) with IgG4-sclerosing cholangitis. IgG4-RD can affect multiple organs in the body, including both the bile ducts and the pancreas in this case. Histologically, IgG4-RD is characterized by a dense lymphoplasmacytic infiltrate with a predominance of IgG4-positive plasma cells. This typically leads to a significant degree of fibrosis. Importantly, serum IgG4 levels may be normal in up to one-third of patients. IgG4 sclerosing cholangitis is important to differentiate from primary sclerosing cholangitis in that it has a much better prognosis and is typically steroid responsive. In contrast, there is no approved medical treatment for primary sclerosing cholangitis. The typical age of onset for IgG4-RD is in the sixth decade, and there is a male predominance. ERCP would not be indicated in this patient as corticosteroids are preferred over stenting, and seldom obtain diagnostic biopsies. Corticosteroids should be initiated prior to any consideration of surgical intervention.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	768	30-120
Bilirubin (total), serum, mg/dL	14.8	0.3-1.0
IgG, mg/dL	2300	800-1500
IgG4, mg/dL	190	10-140

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	296	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	20	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	30	10-40

REFERENCES

Chapman R, Fevery J, Kalloo A, et al. Diagnosis and management of primary sclerosing cholangitis. *Hepatology*. 2010;51(2):660-678. doi:10.1002/hep.23294

Naitoh I, Nakazawa T. Classification and Diagnostic Criteria for IgG4-Related Sclerosing Cholangitis. *Gut Liver*. Published online 2021. doi:10.5009/gnl210116

Question 18

A 32-year-old Black woman presents to you for evaluation of asymptomatic elevations in her liver-associated enzymes. Her total bilirubin level is normal. She has no other past medical history and does not drink alcohol or smoke tobacco. She complains of fatigue and a chronic nonproductive cough. Abdominal ultrasound reveals an enlarged and heterogeneous-appearing liver with patent vasculature as well as splenomegaly. Chest radiography reveals bilateral hilar adenopathy and subtle interstitial changes. Her laboratory results demonstrate the following shown above.

Which of the following would most likely next step to establish this patient's diagnosis?

- A. Measure the angiotensin-converting enzyme level
- B. Obtain a liver biopsy
- C. Magnetic resonance cholangiopancreatography
- D. Response to corticosteroids

CORRECT ANSWER: B

RATIONALE

This patient has hepatic sarcoid. With the liver test abnormalities, liver biopsy may be recommended to

establish the presence of noncaseating granulomas. As clinically important liver injury is rare, treatment with corticosteroids in the absence of symptoms (50-80% of patients are asymptomatic) often does not impact long-term outcomes as it is unclear whether or not steroids prevent, halt, or reverse disease progression. Moreover, there is emerging evidence to suggest weight-based ursodiol (10-15 mg/kg daily) as first-line therapy for 3 months before the initiation of corticosteroids. Hepatic sarcoid alone does not require initiation of treatment with corticosteroids. Although serum angiotensin-converting enzyme level may be elevated in patients with hepatic sarcoid, this is not specific to this condition in that it may be elevated in other diseases. Magnetic resonance cholangiopancreatography would be less helpful with no mention of bile duct dilation on the abdominal ultrasound.

REFERENCES

Kumar M, Herrera JL. Sarcoidosis and the Liver. *Clin Liver Dis*. 2019;23(2):331-343. doi:10.1016/j.cld.2018.12.012

Shah N, Mitra A. Gastrointestinal and Hepatic Sarcoidosis: A Review Article. *Clin Liver Dis*. 2021;17(4):301-307. doi:10.1002/cld.1055

Question 19

A 45-year-old man received a liver transplant from a deceased donor 7 months ago for severe acute alcohol-associated hepatitis that failed to respond to medical treatment.

His initial posttransplantation course was uncomplicated.

Over the past week, his liver-associated enzymes have been repeatedly elevated to reveal results shown at the top on the following page.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	170	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	234	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	150	10-40
Bilirubin (total), serum, mg/dL	1.0	0.3-1.0
International normalized ratio	1.0	<1.1
Tacrolimus, whole blood (trough), ng/mL	<2.0 (Last month, 6.5)	5.0-10.0

Beyond some mild fatigue, he feels well. He takes no other medications besides tacrolimus, including over-the-counter medications or supplements. He denies alcohol consumption, which is confirmed by urine phosphatidyl ethanol testing. Ultrasound with doppler of the liver is normal, and serum cytomegalovirus polymerase chain reaction is undetectable. Magnetic resonance imaging with magnetic resonance cholangiopancreatography does not show any biliary stricture.

Accordingly, you decide to proceed with liver biopsy.

Which of the following would be an expected finding in his liver histology?

- A. Ductopenia and cholestasis
- B. Ductulitis and endotheilitis
- C. Intranuclear inclusions with prominent mononuclear infiltrate
- D. Multinucleated hepatocytes

CORRECT ANSWER: B

RATIONALE

This patient has acute cellular rejection in the setting of a sub-therapeutic tacrolimus drug level. Acute cellular rejection, which may also be called T-cell mediated rejection, is characterized by ductulitis and endotheilitis. Over time, recurrent episodes of albuminuria or chronic under-immunosuppression may lead to chronic rejection, which has very different histologic features. Chronic rejection is characterized by ductopenia and cholestasis in liver tissue. Posttransplantation infections such as cytomegalovirus or herpes simplex virus may lead to intranuclear inclusions and/or multinucleated hepatocytes.

REFERENCES

Banff schema for grading liver allograft rejection: an international consensus document. *Hepatology*. 1997;25(3):658-663. doi:10.1002/hep.510250328

Harrington CR, Yang GY, Levitsky J. Advances in Rejection Management: Prevention and Treatment. *Clin Liver Dis*. 2021;25(1):53-72. doi:10.1016/j.cld.2020.08.003

Question 20

A 68-year-old man underwent a liver transplant from his 23-year-old niece 4 months ago for chronic hepatitis C virus (HCV) cirrhosis and hepatocellular carcinoma. His HCV was treated and cured before transplantation with direct-acting antiviral therapy. His immediate post-liver transplantation course was uneventful as his liver-associated enzymes and liver function normalized soon after transplantation. He now presents to clinic for an unexpected visit complaining of a 3-day history of fevers, chills, and malaise in the setting of profuse diarrhea and a new maculopapular rash on his chest, back, arms, hands, and legs. His current medications include tacrolimus and mycophenolate mofetil for immunosuppression. He also takes sulfamethoxazole-trimethoprim and valganciclovir for routine posttransplantation infection prophylaxis. He is compliant with his medications and does not engage in high-risk behavior. He appears acutely ill on examination. Laboratory testing demonstrates results shown on the following page.

Liver ultrasound with duplex shows expected posttransplantation anatomy, including normal blood flow in the vasculature.

Laboratory Test	Result	Reference Range
Absolute neutrophil count, cells/ μ L	500	2000-8250
Albumin, serum, g/dL	3.5	3.5-5.5
Alkaline phosphatase, serum, U/L	105	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	19	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	15	10-40
Bilirubin (total), serum, mg/dL	0.7	0.3-1.0
Hemoglobin, blood, g/dL	7	14-18
International normalized ratio	0.9	<1.1
Leukocyte count, cells/ μ L	910	4000-11,000
Tacrolimus, ng/mL	8	Target level, 6-8

What is the most likely diagnosis for this patient?

- A. Cytomegalovirus (CMV) infection
- B. Graft-versus-host disease (GvHD)
- C. Recurrent hepatitis C virus (HCV) infection
- D. T-cell mediated rejection

CORRECT ANSWER: B

RATIONALE

This patient is presenting with classic features of GvHD including fevers, diarrhea, and maculopapular rash in the setting of pancytopenia (leukopenia and anemia) and normal liver-associated enzymes. GvHD is most common within the first year after liver transplantation and though it is rare, it is associated with very poor outcomes within 12 months after diagnosis. Risk factors for GvHD after liver transplantation are controversial; however, older recipient age (especially if paired with a younger donor) and hepatocellular carcinoma may increase the risk. Rash, diarrhea, and cytopenia are not characteristic of T-cell mediated rejection and normal liver-associated enzymes also argue against this diagnosis. Although CMV infection can cause diarrhea and cytopenias, it is unlikely to develop this while still receiving CMV prophylaxis with valganciclovir. Recurrent HCV

infection is unlikely with a cure before liver transplantation, especially in the absence of an HCV-positive donor.

REFERENCE

Murali AR, Chandra S, Stewart Z, et al. Graft Versus Host Disease After Liver Transplantation in Adults: A Case series, Review of Literature, and an Approach to Management. *Transplantation*. 2016;100(12):2661-2670. doi:10.1097/tp.0000000000001406

Question 21

A 42-year-old man underwent deceased-donor liver transplantation 2 days ago for cirrhosis secondary to primary sclerosing cholangitis. His organ came from a cytomegalovirus (CMV)-positive donor, and he is CMV-negative. He remains intubated and on vasopressor support in the surgical intensive care unit. Over the past hour, his laboratory test results have continued to worsen and now show the following below.

Ultrasound of the liver with doppler does not show any flow in the main hepatic artery.

What is the most appropriate next step in this patient's clinical management?

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	3568	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	3987	10-40
Arterial blood gas studies (patient breathing room air) - pH	7.20	7.38-7.44
International normalized ratio	4.3	<1.1
Lactate, serum or plasma, mmol/L	5.0	0.7-2.1

- A. Emergent interventional radiology consultation for hepatic artery angiography
- B. Emergent status 1a listing for retransplantation
- C. Emergent surgical re-exploration
- D. Initiate anticoagulation with a heparin drip

CORRECT ANSWER: B

RATIONALE

This patient has developed early hepatic artery thrombosis (HAT) within 7 days of liver transplantation with severe graft dysfunction (aspartate aminotransferase, $\geq 3,000$ IU/L and at least 1 of the following: international normalized ratio, ≥ 2.5 ; arterial pH, ≤ 7.3 ; venous pH, ≤ 7.25 ; or lactate, ≥ 4 mmol/L). Given the high mortality associated with early HAT, he meets criteria for listing as status 1A for urgent retransplantation. At the current moment, he is too unstable to undergo either angiography in the interventional radiology suite or surgical re-exploration with direct examination of his arterial anastomosis to confirm the suspicion of HAT; moreover, no flow was visualized in the main hepatic artery on ultrasound with doppler. He is also too high-risk for bleeding complications to initiate therapeutic anticoagulation within 2 days of liver transplantation, especially with the possibility of imminent re-transplantation. Both primary sclerosing cholangitis and donor CMV infection may increase the risk of HAT following liver transplantation.

REFERENCE

Policies - OPTN. Accessed March 11, 2022.
<https://optn.transplant.hrsa.gov/policies-bylaws/policies/>

Question 22

A 55-year-old man is listed for liver transplantation given his history of cirrhosis secondary to nonalcoholic steatohepatitis. He presents to clinic for his follow-up examination. He has clinically significant portal hypertension with a history of nonbleeding esophageal varices visualized on upper endoscopy 1 year prior but no history of ascites or encephalopathy. He takes nadolol for primary prevention of variceal hemorrhage. He feels well and has no complaints.

After your visit, you obtain updated laboratory test results that are shown below.

He also undergoes a complete abdominal ultrasound for hepatocellular carcinoma screening and is found to have no flow in his main portal vein. Contrasted computed tomography (CT) of the abdomen and pelvis confirms he has an occlusive main portal vein thrombosis (PVT) without evidence of cavernous transformation or collateralization.

What is the next best step in the management of this patient?

- A. Initiate anticoagulation immediately
- B. Perform no intervention and repeat a contrasted CT in 3 months
- C. Remove the patient from the liver transplantation waiting list
- D. Repeat an upper endoscopy and treat large, high-risk esophageal varices if they are present

CORRECT ANSWER: D

RATIONALE

This patient with cirrhosis has a newly diagnosed

Laboratory Test	Result	Reference Range
Bilirubin (total), serum, mg/dL	2.0	0.3-1.0
Creatinine, serum, mg/dL	1.0	0.7-1.5
Hemoglobin, blood, g/dL	12.9	14-18
International normalized ratio	1.4	<1.1
Platelet count, plts/ μ L	99,000	150,000-450,000
Sodium, serum, mEq/L	139	136-145

PVT in the absence of mesenteric ischemia or severe portal hypertension flare and can be managed in the outpatient setting. As he has no other indication for transjugular intrahepatic portosystemic shunt (TIPS) placement (eg, refractory ascites, uncontrolled variceal hemorrhage), the next best step in his clinical management is to perform surveillance upper endoscopy. If he does not have high-risk esophageal varices, treatment with anticoagulation should be initiated; however, if high-risk varices are found, anticoagulation should be delayed while serial band ligation is performed in accordance with best clinical practices until eradication is achieved. Given the associated benefits of intervention either with anticoagulation or TIPS, delaying intervention and repeating an imaging study in 3 months would not improve this patient's outcomes. Historically, PVT was a barrier to successful liver transplantation; however, patients are now given transplants at most liver transplantation centers with PVT, especially when the thrombus is confined to the main portal vein.

REFERENCES

Intagliata NM, Argo CK, Stine JG, Lisman T, Caldwell SH, Violi F. Concepts and Controversies in Haemostasis and Thrombosis Associated with Liver Disease: Proceedings of the 7th International Coagulation in Liver Disease Conference. *Thromb Haemost.* 2018;118(8):1491-1506. doi:10.1055/s-0038-1666861

Northup PG, Garcia-Pagan JC, Garcia-Tsao G, et al. Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by

the American Association for the Study of Liver Diseases. *Hepatology.* 2021;73(1):366-413. doi:10.1002/hep.31646

Question 23

A 31-year-old previously healthy woman presents to the emergency department with 3 days of abdominal pain and abdominal distention. She denies fevers, nausea, vomiting, melena, or hematochezia. She denies any alcohol or drug use. She takes no medications or supplements. On examination, she is alert and oriented. Her heart rate is 110 bpm, blood pressure is 110/70 mmHg, and temperature is 37.2°C. Her abdominal examination shows shifting dullness, fullness at the flanks, and hepatomegaly. Laboratory testing reveals the following results shown below.

Abdominal ultrasound with Doppler shows caudate lobe hypertrophy, no blood flow in the middle hepatic vein, and partial thrombosis of the main portal vein.

Which of the following is the best test to establish this patient's diagnosis?

- A. Factor V Leiden mutation
- B. *JAK2* V617F mutation
- C. Protein C deficiency
- D. Protein S deficiency
- E. Prothrombin gene mutation

CORRECT ANSWER: B

RATIONALE

This patient has Budd-Chiari syndrome (BCS) in

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	220	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	600	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	820	10-40
Bilirubin (total), serum, mg/dL	2.5	0.3-1.0
Hemoglobin, blood, g/dL	18.0	12-16
International normalized ratio	1.2	<1.1
Leukocyte count, cells/ μ L	10,000	4000-11,000
Platelet count, pLts/ μ L	480,000	150,000-450,000

the setting of a polycythemia and thrombocytosis, each of which are hypercoagulable states. BCS is a rare disease and can be *primary* or *secondary* with compression or invasion by a lesion originating outside of the veins from a mass, hepatic abscess or liver cyst. Concomitant PVT is common in patients with BCS. Primary BCS typically occurs in the setting of an underlying risk factor. Myeloproliferative disorders can be found in as many as 50% of patients with BCS. In the absence of a major provoking factor such as in this patient, the following testing should be considered in collaboration with a hematologist: *JAK2* V617F mutation, antiphospholipid antibodies, and flow cytometry to rule out paroxysmal nocturnal hemoglobinuria. If *JAK2* V617F mutation is negative, testing for the *CALR* mutation can be considered. Testing for heritable thrombophilia, such as Factor V Leiden mutation, Protein C or S deficiency or prothrombin gene mutation is not routinely recommended as the results generally do not influence management and Protein C and S can be low in the context of acute thrombosis such as in this patient.

REFERENCE

Northup PG, Garcia-Pagan JC, Garcia-Tsao G, et al. Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):366-413. doi:10.1002/hep.31646

Question 24

A 26-year-old woman with no past medical history presents to the emergency department with 2 weeks of abdominal pain and abdominal fullness. She takes an oral contraceptive for dysmenorrhea and has done so for many years. Ultrasound of the liver with doppler study suggests absence of blood flow in her middle hepatic vein and large volume ascites. She is admitted to the hospital and given the concern for Budd-Chiari syndrome (BCS); she is sent to the interventional radiology suite for a hepatic venogram. This study reveals a

“spider-web” network pattern of venous radicals and a coarse network of collateral veins coalescing between the hepatic vein and the inferior vena cava, confirming the diagnosis of BCS. Her oral contraceptive is discontinued. She undergoes a paracentesis and is then prescribed low molecular weight heparin.

A fluid analysis is completed of this patient's ascites. Which of the following results for the total protein and the calculated serum ascites albumin gradient (SAAG) is most consistent with the patient's disease process?

- A. Total protein, 1.0; SAAG, <1.1 g/dL
- B. Total protein, 1.0; SAAG, >1.1 g/dL
- C. Total protein, 1.1; SAAG, >1.1 g/dL
- D. Total protein, 3.5; SAAG, <1.1 g/dL
- E. Total protein, 3.5; SAAG, >1.1 g/dL

CORRECT ANSWER: E

RATIONALE

BCS is a rare disease in which hepatic venous outflow tract is found. Because the obstruction is post-sinusoidal, this patient would be expected to have evidence of portal hypertension with a SAAG higher than 1.1 g/dL. Patients with early BCS will have ascites protein of 2.5 g/dL or higher; however, as the disease progresses, ascites in patients with late-stage BCS begins to look more like that found in patients with cirrhosis where the ascites protein decrease to lower than 2.5 g/dL.

REFERENCES

Hernaez R, Hamilton JP. Unexplained ascites. *Clinical liver disease*. 2016;7(3):53-56. doi:10.1002/cld.537

Northup PG, Garcia-Pagan JC, Garcia-Tsao G, et al. Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):366-413. doi:10.1002/hep.31646

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.2	3.5–5.5
Alkaline phosphatase, serum, U/L	100	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	167	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	190	10–40
Bilirubin (total), serum, mg/dL	2.0	0.3–1.0
International normalized ratio	1.0	<1.1

Question 25

A 27-year-old man underwent allogeneic hematopoietic stem cell transplantation (HSCT) for acute lymphocytic leukemia. He received high-dose myeloablative chemotherapy with total-body irradiation before this HSCT. He has no prior history of chronic liver disease. A hepatology consultation is requested on day 11 of his hospital stay because he developed right upper quadrant (RUQ) pain, increased abdominal distention, and new onset of painful hepatomegaly. He has gained 10 pounds over the past 2 days. Laboratory testing shows the following shown above.

Abdominal ultrasound reveals enlarged, hypoechoic liver with large volume ascites. Doppler study shows normal flow in both the hepatic and portal veins.

Which of the following medications could have been used prior to HSCT and reduce the risk of this patient's complication?

- A. Defibrotide
- B. N-acetylcysteine
- C. Methylprednisolone
- D. Ursodeoxycholic acid

CORRECT ANSWER: D

RATIONALE

This patient has sinusoidal obstruction syndrome (SOS). SOS is also known as hepatic venoocclusive disease which occurs in the setting of extensive necrosis of liver endothelial cells that extend into the sinusoids, leading to either partial or complete occlusion of the small hepatic venules. SOS is a type of post-sinusoidal portal hypertension that can occur commonly in the setting of

myeloablative chemotherapy with or without total-body irradiation. Prescribing ursodeoxycholic acid the day before myeloablative chemotherapy and continuing this for 3 months after HSCT may be effective in preventing SOS and is recommended for all patients undergoing allogeneic HSCT in particular. Defibrotide is the only SOS treatment approved by the US Food and Drug Administration, and it is prescribed for moderate or severe cases. It does not have a role in preventing SOS. The patient has no history of chronic liver disease. In general, HSCT can be safely performed in patients with chronic liver disease; however, the presence of cirrhosis should prevent the use of myeloablative chemotherapy. A workup for chronic liver disease before HSCT should focus on the exclusion of cirrhosis.

REFERENCES

Northup PG, Garcia-Pagan JC, Garcia-Tsao G, et al. Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):366–413. doi:10.1002/hep.31646

Tay J, Tinmouth A, Fergusson D, Huebsch L, Allan DS. Systematic review of controlled clinical trials on the use of ursodeoxycholic acid for the prevention of hepatic veno-occlusive disease in hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant*. 2007;13(2):206–217. doi:10.1016/j.bbmt.2006.09.012

Question 26

A 55-year-old man is referred to you for evaluation of elevated liver enzymes and abnormal

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	85	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	70	10–40
Ferritin, serum, ng/mL	1600	24–336
Transferrin saturation, %	88	20–50

iron studies. He has the following laboratory test results that are shown above.

His complete blood count is normal. The patient does report fatigue and joint pains that he has attributed to getting older. His physical examination is normal with body mass index of 24 kg/m² and normal blood pressure. He is taking no medications or supplements. He does not drink alcohol. His serologic testing is negative for viral hepatitis, autoimmune hepatitis, and alpha-1-antitrypsin deficiency. He is homozygous for the C282Y mutation. His liver ultrasound with doppler is normal.

What is the next appropriate step in the evaluation of this patient?

- A. Commence phlebotomy
- B. Continue close monitoring and treat when symptoms develop
- C. Obtain magnetic resonance imaging with T2* sequence for hepatic iron quantification
- D. Proceed with liver biopsy

CORRECT ANSWER: D

RATIONALE

The patient’s elevated liver enzymes in the context of elevated iron saturation and elevated ferritin and homozygosity for the C282Y mutation point to a diagnosis of hereditary hemochromatosis. An elevated serum ferritin level greater than 1000 µg/L is associated with increased risk for this patient having advanced hepatic fibrosis or cirrhosis, and he warrants a liver biopsy. Although

phlebotomy is indicated for this patient, completing his evaluation with liver biopsy is the appropriate next step. This patient has elevated liver enzymes and a high serum ferritin in the context of homozygosity for the C282Y mutation and ultimately warrants treatment with phlebotomy once his liver disease has been accurately staged. MRI with quantification of hepatic iron content using T2* sequence can be used but is only recommended in patients that are non-C282Y homozygotes in whom fibrosis staging or exclusion of secondary liver disease is not also indicated. Transient elastography is not yet validated for fibrosis staging in hereditary hemochromatosis.

REFERENCE

Kowdley K v., Brown KE, Ahn J, Sundaram V. ACG Clinical Guideline: Hereditary Hemochromatosis. *Am J Gastroenterol.* 2019;114(8):1202-1218. doi:10.14309/ajg.0000000000000315

Question 27

You are evaluating a chronically ill 58-year-old man with a 5-year history of elevated liver enzymes.

Laboratory tests include the following results shown below.

His past medical history is notable for diabetes mellitus and hypothyroidism as well as ischemic heart disease with congestive heart failure. His main clinical complaints are fatigue and loss of libido. Over the course of an extensive evaluation,

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	96	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	87	10–40
Ferritin, serum, ng/mL	1131	24–336
Transferrin saturation, %	67	20–50

a liver biopsy is performed that reveals 2+ intra-hepatic iron staining, with stage 2 to 3 fibrosis. The patient presents now for recommendations regarding his elevated ferritin and consideration of phlebotomy. *HFE* gene mutation testing shows no mutations present.

Which of the following statements regarding the patient's diagnostic workup and treatment of his iron overload is true?

- A. Additional genetic testing to exclude non-*HFE* gene mutations; if positive, start phlebotomy
- B. Magnetic resonance imaging to evaluate for hepatic iron overload; if present, start phlebotomy
- C. No additional testing is required; patient should begin phlebotomy
- D. No additional testing is required; patient should NOT begin phlebotomy

CORRECT ANSWER: D

RATIONALE

Secondary iron overload is common in other causes of chronic liver disease, particularly with alcohol-associated liver disease and nonalcoholic fatty liver disease. Both of these conditions can cause elevation in iron binding saturation as well as ferritin, often to a similar degree as one may suspect for hemochromatosis. Testing for non-*HFE* gene mutations is not recommended unless there is no alternative explanation or if presentation raises concern (eg, younger patient, other unexplained end-organ disease). Phlebotomy is reserved for patients with a genetic diagnosis of hereditary hemochromatosis, not those with define causes of secondary iron overload. Although magnetic resonance imaging can be helpful to

quantify the extent of hepatic iron overload, in this case, it would provide no additional clinical information. Biopsy would reveal iron deposition in the reticuloendothelial system consistent with secondary iron overload.

REFERENCE

Kowdley K v., Brown KE, Ahn J, Sundaram V. ACG Clinical Guideline: Hereditary Hemochromatosis. *Am J Gastroenterol.* 2019;114(8):1202-1218. doi:10.14309/ajg.0000000000000315

Question 28

A 23-year-old woman presents to you for evaluation of elevated liver enzymes. She is originally from East Africa and has a family history of liver disease and heart failure of unclear etiology.

Her laboratory results include the following shown below. *HFE* gene mutation testing is negative, but liver biopsy confirms significant iron deposition in the hepatocytes (hepatic iron index, 2.7).

Which subtype of hereditary hemochromatosis (HH) is most likely present in this patient?

- A. Hemochromatosis type 1
- B. Hemochromatosis type 2
- C. Hemochromatosis type 3
- D. Hemochromatosis type 4

CORRECT ANSWER: D

RATIONALE

Hemochromatosis is subdivided into 4 types based on genetic mutations present. Type 1 (hereditary) represents disease due to *HFE* gene mutations and comprises 95% of all HH cases. Non-*HFE*

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	72	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	68	10–40
Ferritin, serum, ng/mL	868	24–336
Transferrin saturation, %	91	20–50

gene mutation types of hemochromatosis include type 2 to 4 and occur in less than 5% of cases. All gene mutations impact the hepcidin-ferroportin axis. Hepcidin is produced by the liver and acts on enterocytes and macrophages to provide negative feedback to block ferroportin excretion of iron into the blood stream. Type 1, 2 (juvenile), and 3 (TFR-related) hemochromatosis all involve genetic defects that impair synthesis or function of hepcidin resulting in low hepcidin levels and loss of negative feedback regulation of ferroportin excretion of iron into the circulation. Type 4 (ferroportin disease) hemochromatosis involves mutations in ferroportin itself, making it no longer susceptible to the negative feedback signal of hepcidin, and therefore, results in a high level of hepcidin but with excess iron excreted into the circulation. Notably, type 4 hemochromatosis is autosomal dominant and though rare, it is prevalent in African countries. Mutations in the *SLC40A* gene for ferroportin impact disease presentation; however, in instances where tissue iron overload is confirmed, as in this case, phlebotomy is indicated.

REFERENCES

Kowdley K v., Brown KE, Ahn J, Sundaram V. ACG Clinical Guideline: Hereditary Hemochromatosis. *Am J Gastroenterol.* 2019;114(8):1202-1218. doi:10.14309/ajg.0000000000000315

Kowdley KV, Trainer TD, Saltzman JR, et al. Utility of hepatic iron index in American patients with hereditary hemochromatosis: a multicenter study. *Gastroenterology.* 1997;113(4):1270-1277. doi:10.1053/gast.1997.v113.pm9322522

Pietrangelo A. Ferroportin disease: Pathogenesis, diagnosis and treatment. *Haematologica.* 2017;102(12):1972-1984. doi:10.3324/haematol.2017.170720

Question 29

A 31-year-old woman returns from a safari trip in sub-Saharan Africa. The patient is diagnosed with portal hypertension due to a parasitic infection.

Which of the following combinations of portal pressure measurements (the wedged hepatic venous pressure [WHVP], the free hepatic venous pressure [FHVP], and the hepatic venous pressure gradient [HVPG]) would be expected in this patient?

- A. WHVP is low; FHVP is low; HVPG is normal
- B. WHVP is high; FHVP is high; HVPG is normal
- C. WHVP is high; FHVP is normal; HVPG is high
- D. WHVP is normal; FHVP is normal; HVPG is normal

CORRECT ANSWER: D

RATIONALE

This patient has a diagnosis of schistosomiasis. Schistosomiasis and deposition of the oocytes in the presinusoidal portal venules causes an intrahepatic, pre-sinusoidal portal hypertension. The HVPG is calculated by subtracting the FHVP from the WHVP. This is characterized by normal WHVP, normal FHVP, and normal HVPG. Sinusoidal portal hypertension (such as cirrhosis) has an elevated WHVP, normal FHVP, and elevated HVPG. Posthepatic portal hypertension (such as right heart failure), has an elevated WHVP, elevated FHVP, and resultant normal HVPG. Prehepatic portal hypertension from an occlusive portal vein thrombosis with limited flow into the liver, though typically this is diagnosed based on cross-sectional imaging, not HVPG measurement.

REFERENCE

Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2017;65(1):310-335. doi:10.1002/hep.28906

Question 30

A 23-year-old previously healthy woman presents with new-onset abdominal pain, abdominal distention, and lower extremity edema. She has no

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	214	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	211	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	256	10-40
Bilirubin (total), serum, mg/dL	1.3	0.3-1.0
International normalized ratio	1.0	<1.1

past medical history. Her only medication is oral contraceptive pills. She takes no supplements. She does not smoke or drink alcohol.

Her laboratory test results reveal the following shown above.

Serologic testing is negative for viral and autoimmune hepatitis. Pregnancy test is negative. On physical examination, her abdomen is distended with a discernable fluid wave. She has 1+ bilateral lower extremity edema. She is alert and oriented x 4 with no asterixis.

Which of the following is the next most appropriate test to make the diagnosis?

- A. Hepatic arteriogram
- B. Hepatic ultrasound with Doppler
- C. Liver biopsy
- D. Magnetic resonance cholangiopancreatography

CORRECT ANSWER: B

RATIONALE

This patient has signs and symptoms most consistent with acute Budd-Chiari syndrome (BCS) with new-onset ascites and elevated liver enzymes. Hepatic ultrasound with doppler is the next appropriate test to assess the patency of the hepatic veins and inferior vena cava. BCS is a hepatic venous outflow derangement; therefore, hepatic arteriogram would not be a reasonable next test.

Magnetic resonance cholangiopancreatography assesses the biliary tree and would not be the next best test. Liver biopsy is invasive and is rarely indicated for the initial diagnosis of symptomatic Budd-Chiari syndrome. Importantly, though this patient presented acutely, clinical presentation can vary including acute liver failure (in those with rapid formation of occlusive thrombus), cirrhosis from chronic asymptomatic disease, and asymptomatic disease incidentally found on imaging.

REFERENCE

Northup PG, Garcia-Pagan JC, Garcia-Tsao G, et al. Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):366-413. doi:10.1002/hep.31646

Question 31

A 21-year-old woman presents to emergency department with abdominal pain and jaundice. Her only medication is oral contraceptives. Initial laboratory results are shown below.

Ultrasound of the liver confirms absence of flow in her hepatic vein consistent with Budd-Chiari syndrome (BCS) and associated hepatomegaly with ascites. She prescribed intravenous heparin without improvement over the next 72 hours.

What is the next best step in her management?

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	230	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	1221	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	998	10-40
Bilirubin (total), serum, mg/dL	1.2	0.3-1.0
International normalized ratio	1.3	<1.1

- A. Liver transplantation
- B. Surgical shunt
- C. Switch to alternative anticoagulant
- D. Transjugular intrahepatic portosystemic shunt

CORRECT ANSWER: D

RATIONALE

This patient is presenting with symptoms and laboratory results consistent with acute BCS confirmed on diagnostic ultrasound. Treatment of BCS involves a step-wise progression, initially with medical therapy and consideration of endovascular treatments including angioplasty and TIPS if this fails. Liver transplantation should be reserved as a last resort in patients who have not responded to this step-wise approach. In this case, the patient is not responding to initial anticoagulation as evident by persistent ascites and still elevated laboratory results warrant consideration of endovascular treatment options. In this case, TIPS would be favored. In fact, with the introduction of polytetrafluoroethylene (PTFE) coated stents, this can be a durable therapy and in one study, 72% of patients remained transplant-free at 5 years. Although surgical shunts remain an option, this approach has largely been replaced given the wide availability of transjugular intrahepatic portosystemic shunt and advances in durability of PTFE-coated stents. Liver transplantation should be reserved for those patients who remain refractory despite endovascular therapy.

REFERENCES

Northup PG, Garcia-Pagan JC, Garcia-Tsao G, et al. Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients

With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):366-413. doi:10.1002/hep.31646

Seijo S, Plessier A, Hoekstra J, et al. Good long-term outcome of Budd-Chiari syndrome with a step-wise management. *Hepatology*. 2013;57(5):1962-1968. doi:10.1002/hep.26306

Question 32

A 57-year-old man presents to the emergency department with a complaint of right upper quadrant (RUQ) pain, fever, chills, and jaundice for 5 days. He reports no dysphagia or odynophagia, no diarrhea or constipation. His vital signs are as follows: heart rate, 100 bpm and regular; blood pressure, 145/70 mmHg; respiratory rate, 14 breaths per minute; oxygen saturation 98% on room air. His examination is remarkable for moderately tender hepatomegaly.

Laboratory tests reveal the following shown below.

RUQ ultrasound revealed a normal gallbladder without gallstones, pericholecystic fluid, and gallbladder wall thickening. His common bile duct was 3 mm, the liver was enlarged, and no liver masses were seen. The spleen was also mildly enlarged. Doppler study showed normal flow in the hepatic and portal veins. Upon questioning, his family reports that he drinks 1 to 2 pints of hard liquor daily.

Which of the following treatments is the best option for this patient?

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.0	3.5-5.5
Alkaline phosphatase, serum, U/L	110	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	88	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	143	10-40
Bilirubin (total), serum, mg/dL	9.1	0.3-1.0
Hemoglobin, blood, g/dL	12.1	14-18
International normalized ratio	1.6	<1.1
Leukocyte count, cells/ μ L	16,100	4000-11,000
Platelet count, plts/ μ L	147,000	150,000-450,000

- A. Corticosteroids
- B. Liver transplantation
- C. N-acetylcysteine
- D. Pentoxifylline

CORRECT ANSWER: A

RATIONALE

In a patient with a history of heavy alcohol use, the diagnosis of acute alcohol-associated hepatitis (AH) is suggested by the onset or sudden worsening of jaundice with or without other signs of hepatic dysfunction. Physical examination in AH may reveal stigmata of liver cirrhosis, as well as systemic inflammatory response syndrome criteria, due to the significant inflammatory response in the liver. Laboratory findings include an elevated bilirubin, and an AST/ALT ratio greater than 1.5 with a total AST or ALT less than 400 IU/L. Biopsy is not typically performed, but will show macrovesicular steatosis, a neutrophilic lobulitis, the presence of Mallory-Denk bodies, and pericellular fibrosis. Unfortunately, these findings are also seen in nonalcoholic steatohepatitis, so an alcohol history is a crucial part of the workup. Current guidelines define “Definite AH” by the biopsy findings but allow a diagnosis of “Probable AH” if the following criteria are met: 1) Heavy alcohol use for greater than 5 years; 2) active alcohol use until 4 weeks before presentation; 3) sudden onset or worsening of jaundice; 4) AST/ALT greater than 1.5 with levels less than 400 IU/L; and 5) absence of other causes of liver disease. In patients with AH, prognosis can be estimated using the Model for End-Stage Liver Disease (MELD) score or the Maddrey Discriminant Function (DF); a DF greater than 32 predicts a 20-50 percent 30-day mortality and patients meet-

ing this threshold should be treated as by definition they have severe AH. Current US guidelines call for the use of corticosteroids (specifically prednisolone) in severe AH. Response to steroid therapy is assessed at day 4 or 7 using the Lille score, with therapy continued for a total of 28 days in initial responders. Pentoxifylline had shown possible benefit in earlier studies, but more recent data show no benefit, and this is no longer recommended in the most recent US guidelines. There is limited data to support the addition of N-acetylcysteine to corticosteroids in AH, though there is no role for this agent as a monotherapy. Liver transplantation for AH should be considered, but only in patients refractory to medical therapy.

REFERENCE

Crabb DW, Im GY, Szabo G, Mellinger JL, Lucey MR. Diagnosis and Treatment of Alcohol-Associated Liver Diseases: 2019 Practice Guidance From the American Association for the Study of Liver Diseases. *Hepatology*. 2020;71(1):306-333. doi:10.1002/hep.30866

Question 33

A 37-year-old woman with a history of alcohol dependence presents to the emergency department with a complaint of right upper quadrant (RUQ) pain, fevers and chills, and jaundice for 5 days. She reports no dysphagia or odynophagia, no diarrhea or constipation. Her vital signs are as follows: heart rate, 92 bpm and regular; blood pressure, 145/70 mmHg; respiratory rate, 14 breaths per minute; oxygen saturation, 98% on room air. Her examination is remarkable for moderately tender hepatomegaly. Laboratory tests reveal the following:

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.0	3.5-5.5
Alkaline phosphatase, serum, U/L	110	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	88	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	143	10-40
Bilirubin (total), serum, mg/dL	11.2	0.3-1.0
Hemoglobin, blood, g/dL	12.1	12-16
International normalized ratio	1.6	<1.1
Leukocyte count, cells/ μ L	16,100	4000-11,000
Platelet count, pLts/ μ L	147,000	150,000-450,000

RUQ ultrasound revealed a normal gall bladder without gallstones, pericholecystic fluid, or gall bladder wall thickening. Common bile duct was 3 mm, liver was enlarged, and no liver masses were seen. Doppler study showed normal flow in the hepatic and portal veins. Spleen was mildly enlarged.

A liver biopsy would most likely show which of the following?

- A. Ballooning degeneration and Mallory bodies
- B. Extensive fibrosis with minimal inflammation
- C. Granulomatous inflammation
- D. Lymphoplasmacytic infiltration with rosettes
- E. Periodic acid-Schiff–positive, diastase-resistant globules in hepatocytes

CORRECT ANSWER: A

RATIONALE

In a patient with a history of heavy alcohol use, the diagnosis of acute alcohol-associated hepatitis (AH) is suggested by the onset or sudden worsening of jaundice with or without other signs of hepatic dysfunction. Physical examination in AH may reveal stigmata of liver cirrhosis, as well as systemic inflammatory response syndrome criteria, due to the significant inflammatory response in the liver. Laboratory findings include an elevated bilirubin, and an AST/ALT ratio greater than 1.5 with a total AST or ALT less than 400 IU/L. Biopsy is not typically performed, but if pursued, will show macrovesicular steatosis, a neutrophilic lobulitis, the presence of Mallory bodies, and pericellular fibrosis. Unfortunately, these findings are also seen in nonalcoholic steatohepatitis, so obtaining an accurate and thorough alcohol history is a crucial part of the workup. Importantly,

biopsies in AH add no additional prognostic value beyond clinical scores, such as Maddrey Discriminant Function or Model for End-Stage Liver Disease (MELD) score.

REFERENCE

Forrest E, Petts G, Austin A, et al. The diagnostic and prognostic significance of liver histology in alcoholic hepatitis. *Aliment Pharmacol Ther.* 2021;53(3). doi:10.1111/apt.16157

Question 34

A 50-year-old man presents to clinic with a complaint of fatigue. He drinks approximately 1 pint of whiskey daily and has done so for more than 20 years. His examination is remarkable for hepatomegaly, palmar erythema, and spider angiomas of his neck and chest, but no asterixis or altered mental functioning.

Liver enzyme testing reveals results shown below.

Right upper quadrant ultrasound revealed a normal gallbladder without gallstones, pericholecystic fluid, and gallbladder wall thickening. The common bile duct was 4 mm, liver was small and nodular, no liver masses were seen, and Doppler study showed normal flow in the hepatic and portal veins. The spleen was mildly enlarged.

Which of the following will lead to the greatest improvement in this patient’s survival?

- A. Abstinence
- B. Corticosteroids
- C. Infliximab
- D. Pentoxifylline
- E. Ursodeoxycholic acid

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.0	3.5-5.5
Alkaline phosphatase, serum, U/L	110	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	60	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	110	10-40
Bilirubin (total), serum, mg/dL	1.8	0.3-1.0
International normalized ratio	1.2	<1.1

CORRECT ANSWER: A**RATIONALE**

This patient has stigmata of cirrhosis on examination and laboratory tests indicative of mild synthetic dysfunction. His history of alcohol use and his transaminases (AST/ALT ratio >1.5 is suggestive of alcohol-associated liver disease [ALD]).

He does not have severe acute alcohol-associated hepatitis (AH); therefore, corticosteroids are not indicated and have shown only modest short-term survival benefits when indicated. Pentoxifylline is not currently recommended for AH, and tumor necrosis factor alpha inhibitors have been shown to cause high rates of infection in acute AH and are not used. Ursodeoxycholic acid has no benefit in ALD. Abstinence from alcohol has been shown to correlate with outcomes in ALD, and complete abstinence is the most important factor in management. In patients with alcohol-associated cirrhosis, baclofen has been shown to be safe and to increase abstinence rates, while other abstinence-inducing agents such as acamprosate and naltrexone have possible hepatotoxicity in patients with ALD.

REFERENCE

Singal AK, Bataller R, Ahn J, Kamath PS, Shah VH. ACG clinical guideline: Alcoholic liver disease. *American Journal of Gastroenterology*. 2018;113(2):175-194. doi:10.1038/ajg.2017.469

Question 35

A 31-year-old woman presents to the hospital with severe acute alcohol-associated hepatitis (AH). Her initial laboratory results are as follows:

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	203	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	47	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	155	10-40
Bilirubin (total), serum, mg/dL	14.6	0.3-1.0
Creatinine, serum, mg/dL	0.5	0.7-1.5
International normalized ratio	1.8	<1.1
Platelet count, <i>plts</i> /μL	322,000	150,000-450,000

Her Maddrey Discriminant Function is 50, and she is started on prednisolone 40 mg by mouth daily.

Which of the following outcomes is most likely to improve with her current therapy?

- A. 28-day mortality
- B. 90-day mortality
- C. 90-day transplant-free survival
- C. 1-year mortality

CORRECT ANSWER: A**RATIONALE**

The STOP-AH Trial was a multicenter, double-blind, randomized trial with a 2-by-2 factorial design to evaluate the effect of treatment with prednisolone or pentoxifylline. The primary end point of the study was 28-day mortality with secondary end points that included 90-day and 1-year mortality as well as rate of infection. There was a reduction in 28-day mortality in the prednisolone group, though this was not statistically significant (odds ratio, 0.72; 95% confidence interval, 0.52-1.01; $P = .06$). There was no difference in 90-day or 1-year mortality with prednisolone compared with placebo. Rates of infection were higher in the prednisolone group compared with placebo (13% vs 7%, $P < .01$) and infection should be excluded before considering prednisolone. Importantly, pentoxifylline showed no mortality benefit at any of the study time points.

REFERENCE

Thursz MR, Richardson P, Allison M, et al. Prednisolone or Pentoxifylline for Alcoholic Hepatitis. *N Engl J Med*. 2015;372(17):1619-1628. doi:10.1056/nejmoa1412278

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	2.1	3.5–5.5
Aminotransferase, serum alanine (ALT, SGPT), U/L	56	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	223	10–40
Bilirubin (total), serum, mg/dL	24.3	0.3–1.0
Creatinine, serum, mg/dL	0.4	0.7–1.5
Hemoglobin, blood, g/dL	8.4	14–18
International normalized ratio	2.1	<1.1
Leukocyte count, cells/ μ L	16,300	4000–11,000
Mean corpuscular volume, fL	112	80–98

Question 36

A 37-year-old man with no past medical history presents with new-onset ascites and jaundice. His initial laboratory results are shown above.

Additional history reveals a heavy alcohol use history (12 beers daily x 10 years) until 2 weeks ago when he first noted yellowing of his eyes. His Maddrey Discriminant Function is 98. After infection is excluded, he is prescribed prednisolone 40 mg by mouth daily. Four days later, his bilirubin is 26.1 mg/dL.

What is the next best step in management?

- A. Continue prednisolone 40 mg by mouth daily for 28 days
- B. Evaluate for liver transplantation
- C. Stop prednisolone
- D. Switch to pentoxifylline

CORRECT ANSWER: C

RATIONALE

This patient met criteria for severe acute alcohol-associated hepatitis (AH) and was prescribed prednisolone. Given increased risk of infection in patients with severe AH receiving prednisolone, steroid responsiveness should be assessed to avoid prolonged exposure if clinically nonresponsive. The Lille Model was developed to assess steroid responsiveness and calculates a score between 0 and 1 based on patient age, laboratory test results on day 1 (albumin, prothrombin time, creatinine, and bilirubin) and bilirubin laboratory test results on day 7. A Lille Score greater than 0.45 is consis-

tent with a steroid nonresponder; in these patients, treatment should be stopped. This patient’s Lille Score is 0.71. Subsequent data from the same cohort validated use of day 4 bilirubin to allow for even earlier determination of steroid nonresponse.

The STOP-AH Trial showed that pentoxifylline provides no mortality benefit and would not be a second-line agent in steroid nonresponders. Early liver transplantation for AH has been studied and may be a consideration if patient fails to further improve with abstinence.

REFERENCES

Garcia-Saenz-De-Sicilia M, Duvoor C, Altamirano J, et al. A Day-4 Lille Model Predicts Response to Corticosteroids and Mortality in Severe Alcoholic Hepatitis. *Am J Gastroenterol*. 2017;112(2):306-315. doi:10.1038/ajg.2016.539

Louvet A, Naveau S, Abdelnour M, et al. The Lille model: A new tool for therapeutic strategy in patients with severe alcoholic hepatitis treated with steroids. *Hepatology*. 2007;45(6):1348-1354. doi:10.1002/hep.21607

Question 37

You are consulted for consideration of liver transplantation (LT) for a 24-year-old woman with severe acute alcohol-associated hepatitis.

She was a nonresponder to prednisolone and remains hospitalized with a MELD (Model for End-Stage Liver Disease) score of 40, based on the laboratory results shown on the following page.

Laboratory Test	Result	Reference Range
Bilirubin (total), serum, mg/dL	37	0.3-1.0
Creatinine, serum, mg/dL	1.5	0.7-1.5
International normalized ratio	4.3	<1.1
Sodium, serum, mEq/L	127	136-145

Her last drink of alcohol was 62 days ago, before which she was drinking six 1.5-ounce shots of liquor daily since age 15. She had never received medical care for alcohol-related conditions, nor had she ever been told she had an alcohol use disorder. She is single, lives alone, and works as an accountant. She has no history of legal problems related to her prior alcohol use. She has no history of uncontrolled mental illness.

Which of the following factors is most likely to lead to alcohol relapse in this patient?

- A. Lack of spouse/partner
- B. Lack of prior engagement in the healthcare system
- C. Quantity of daily alcohol use
- D. Sobriety <3 months
- E. Sobriety <6 months

CORRECT ANSWER: A

RATIONALE

Prediction of alcohol use relapse after liver transplantation remains difficult to predict. For prediction before LT, several scoring systems have been developed including the Michigan alcoholism prognostic scale, the high-risk alcoholism relapse, the “Alcohol Relapse Risk Assessment,” and the Stanford Integrated Psychosocial Assessment for Transplantation. These scoring systems share several common themes. Factors favorable to sustained sobriety include strong social support from spouse or partner and insight into alcohol use disorder; those predictive of relapse include failed rehabilitation attempts or co-existent psychiatric disorders. For this patient, lack of a spouse or partner would be a negative factor regarding relapse risk. Importantly, though duration of sobriety before LT is associated with continued sobriety

after LT, no prespecified time point (eg, “6-month rule”) has been predictive of post-LT alcohol use. The Sustained Alcohol Use Post-Liver Transplant (SALT) score was developed to predict post-LT relapse from the cohort of patients who underwent early liver transplantation for severe acute alcohol-associated hepatitis in the ACCELERATE-AH cohort. The variables include greater than 10 drinks daily at initial presentation (4 points), multiple prior rehabilitation attempts (4 points), prior alcohol-associated legal issues (2 points), and prior illicit substance use (1 point), with a composite SALT score lower than 5, having a 95% negative predictive value (95% confidence interval, 89%-98%) for sustained alcohol use following LT, though further validation is still needed.

REFERENCES

- de Gottardi A, Spahr L, Gelez P, et al. A simple score for predicting alcohol relapse after liver transplantation: results from 387 patients over 15 years. *Arch Intern Med.* 2007;167(11). doi:10.1001/archinte.167.11.1183
- Lee BP, Vittinghoff E, Hsu C, et al. Predicting Low Risk for Sustained Alcohol Use After Early Liver Transplant for Acute Alcoholic Hepatitis: The Sustained Alcohol Use Post-Liver Transplant Score. *Hepatology (Baltimore, Md).* 2019;69(4). doi:10.1002/hep.30478
- Maldonado JR, Dubois HC, David EE, et al. The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT): a new tool for the psychosocial evaluation of pre-transplant candidates. *Psychosomatics.* 53(2). doi:10.1016/j.psych.2011.12.012
- Rodrigue JR, Hanto DW, Curry MP. The Alcohol Relapse Risk Assessment: a scoring system to

predict the risk of relapse to any alcohol use after liver transplant. *Prog Transplant*. 2013;23(4). doi:10.7182/pit2013604

Yates WR, Booth BM, Reed DA, Brown K, Masterson BJ. Descriptive and predictive validity of a high-risk alcoholism relapse model. *J Stud Alcohol*. 1993;54(6). doi:10.15288/jsa.1993.54.645

Question 38

A 51-year-old man with an 8-year history of alpha-1 antitrypsin (A1AT) deficiency is found to have the following laboratory results shown below.

Liver biopsy shows established cirrhosis and periodic acid-Schiff (PAS)-positive, diastase-resistant globules in the hepatocytes.

What is the mechanism of liver injury in this disorder?

- A. Deficient A1AT leads to hepatocyte damage by enzymes that would normally be deactivated by this enzyme
- B. Deficient A1AT leads to neutrophilic infiltration of the liver and hepatocyte necrosis
- C. Excess misfolded A1AT accumulates in the liver, leading to lymphocytic infiltration of the liver and subsequent fibrosis
- D. Excess misfolded A1AT accumulates in the liver, leading to oxidative damage to hepatocytes

CORRECT ANSWER: D

RATIONALE
A1AT deficiency is a common metabolic cause of

liver disease in children and adults, affecting approximately 1 in 3500 live births. Production of a misfolded A1AT protein leads to low A1AT levels in the serum (<15% of normal), which leads to lung damage via the unopposed action of pulmonary neutrophil elastase. In the liver, however, damage is caused by accumulation of the abnormal protein in the endoplasmic reticulum of hepatocytes, causing oxidative damage and eventual fibrosis and cirrhosis. On biopsy, the misfolded protein appears as PAS-positive globules within hepatocyte that are resistant to digestion with diastase. A1AT should be suspected in any patient with unexplained cirrhosis or unexplained mild elevations of AST and ALT. A clinical clue to A1AT deficiency is a personal or family history of early chronic obstructive pulmonary disease (before age 50). Although a low A1AT level in the serum can suggest the diagnosis, this enzyme is an acute phase reactant and the A1AT level may be falsely elevated in the setting of inflammation. The gold standard of diagnosis is A1AT phenotyping using isoelectric focusing. This testing allows identification of the abnormally folded protein (the S or Z forms) instead of the normal protein (the M form). Patients with the P*ZZ phenotype express 10 to 20 percent of the normal A1AT and tend to have the most severe disease.

REFERENCE
de Gottardi A, Spahr L, Gelez P, et al. A simple score for predicting alcohol relapse after liver transplantation: results from 387 patients over 15 years. *Arch Intern Med*. 2007;167(11). doi:10.1001/archinte.167.11.1183

Townsend SA, Edgar RG, Ellis PR, Kantas D, Newsome PN, Turner AM. Systematic review: the

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.0	3.5-5.5
Alkaline phosphatase, serum, U/L	105	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	105	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	92	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0
International normalized ratio	1.2	<1.1
Platelet count, plts/ μ L	102,000	150,000-450,000

natural history of alpha-1 antitrypsin deficiency, and associated liver disease. *Aliment Pharmacol Ther.* 2018;47(7). doi:10.1111/apt.14537

Question 39

A 39-year-old man, with an 8-year history of chronic obstructive pulmonary disease (COPD), is found to have the following laboratory results shown below.

He is a current smoker (1 pack per day) and drinks 2 to 3 beers most days within increased use on weekends. Right upper quadrant ultrasound revealed a normal gallbladder with no gallstones, common bile duct was 3 mm, liver was of small size with a nodular contour, no liver masses were seen, and Doppler study showed normal flow in the hepatic and portal veins. Moderate splenomegaly was present. Hepatitis serologies, anti-nuclear antibody, anti-smooth muscle antibodies, iron studies, and serum ceruloplasmin are all negative, but an alpha-1-antitrypsin level (A1AT) is less than 10.

Which of the following tests will reveal the likely cause of this patient's liver disease?

- A. 24-hour urine copper
- B. A1AT phenotyping
- C. Antimitochondrial antibody
- D. C282Y mutation analysis
- E. Phosphatidylethanol level

CORRECT ANSWER: E

RATIONALE

This patient has laboratory testing and imaging

consistent with cirrhosis. Although in this case, the patient does have pulmonary disease from A1AT deficiency likely exacerbated by smoking, the absence of detectable SERPINA1 protein suggests a null mutation. In patients with A1AT deficiency from null mutation, pulmonary disease exists in the absence of liver disease since no protein is present. This differs from PI*ZZ or other abnormal mutation compound heterozygotes for which serum levels of A1AT remain low with accumulation of abnormal protein in the liver that drives hepatic inflammation. In this case, his alcohol use has been significant and is the likely cause of his underlying liver disease, a finding that could be confirmed with phosphatidylethanol testing. Phosphatidylethanol is a metabolite of ethanol that is incorporated in red blood cell membranes and is sensitive enough to detect moderate-heavy alcohol use in the past 30 days. Given normal iron studies, hemochromatosis is unlikely and additional *HFE* gene mutation testing is not indicated. Liver enzymes are not consistent with primary biliary cholangitis and therefore antimitochondrial antibody testing is not indicated. Given normal ceruloplasmin, additional 24-hour urine copper testing is not indicated.

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Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.0	3.5–5.5
Alkaline phosphatase, serum, U/L	105	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	32	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	65	10–40
Bilirubin (total), serum, mg/dL	0.9	0.3–1.0
International normalized ratio	1.2	<1.1
Platelet count, <i>plts</i> /μL	99,000	150,000–450,000

Question 40

A 27-year-old woman who was recently treated for a urinary tract infection presents to your clinic with jaundice. Other than her antibiotic and occasional acetaminophen use for chronic knee pain, she denies any other new medications, herbals, supplements, or illicit drug use. She is jaundiced but with no stigmata of end-stage liver disease nor signs of encephalopathy. Initial laboratory results are shown below.

Initial testing includes abdominal ultrasound that shows mild hepatomegaly with coarsened echotexture, patent hepatic and portal veins, and no splenomegaly or other signs of portal hypertension. Subsequent serologic testing is performed, and the following tests are negative: autoimmune hepatitis (antinuclear antibody, anti-smooth muscle antibody), Wilson’s disease (ceruloplasmin), and acute viral hepatitis (hepatitis A, B, and C viruses, including polymerase chain reaction). Laboratory results fail to improve over the next week and a liver biopsy is performed that shows interface hepatitis with predominance of plasma cells without fibrosis.

Which of the following medications is the likely cause of this patient’s hepatitis?

- A. Amoxicillin
- B. Ciprofloxacin
- C. Fosfomycin
- D. Nitrofurantoin

CORRECT ANSWER: D

RATIONALE

This patient’s biopsy has classic features of auto-

immune hepatitis (AIH), that is drug-induced and related to nitrofurantoin used to treat her recent urinary tract infection in this case. Drug-induced AIH has been reported for several medications including minocycline, statins, anti-tumor necrosis factor alpha agents (eg, infliximab), hydralazine, methyldopa, and diclofenac, though this is most commonly due to either nitrofurantoin or minocycline use. Antibody testing is variable in these patients and diagnosis most often requires liver biopsy that shows classic features of AIH including abundance of plasma cells and interface hepatitis. Treatment for drug-induced AIH requires removal of offending agent (if not yet stopped) and in most instances, treatment with glucocorticoids is required, but longer-term treatment with additional steroid-sparing agents (eg, azathioprine) is generally not necessary. A relapse after immunosuppression withdrawal should prompt consideration of *de novo* AIH. Although autoimmune antibodies are often negative, these can be positive in addition to elevated immunoglobulin G (IgG), which is nonspecific but is commonly elevated in AIH.

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Mack CL, Adams D, Assis DN, et al. Diagnosis and Management of Autoimmune Hepatitis in Adults and Children: 2019 Practice Guidance and Guidelines From the American Association for the Study of Liver Diseases. *Hepatology*. 2020;72(2):671-722. doi:10.1002/hep.31065

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	102	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	782	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	671	10-40
Bilirubin, serum		
Total, mg/dL	6.1	0.3-1.0
Direct, mg/dL	3.1	0.1-0.3
International normalized ratio	1.0	<1.1
Platelet count, plts/ μ L	299,000	150,000-450,000

Question 41

A 13-year-old girl with a history of hypothyroidism due to autoimmune thyroiditis presents to the emergency department with a complaint of fatigue and jaundice. Her examination is remarkable for moderate right upper quadrant (RUQ) tenderness on palpation.

Laboratory results are shown below.

RUQ ultrasound revealed a normal gallbladder with no gallstones, pericholecystic fluid, or gallbladder wall thickening. Common bile duct was 3 mm, and liver was normal in size, contour, and echotexture with no masses. Doppler study showed normal flow in the hepatic and portal veins. Spleen size was normal.

Which of the following antibodies would likely be positive in this patient?

- A. Anti-liver kidney microsome type 1 (anti-LKM1) antibody
- B. Antimitochondrial antibody (AMA)
- C. Antinuclear antibody (ANA)
- D. Anti-soluble liver antigen (anti-SLA1) antibody
- E. Anti-smooth muscle antibody (anti-SMA)

CORRECT ANSWER: A

RATIONALE

This patient is presenting with a clinical picture highly suspicious for type 2 autoimmune hepatitis (AIH). Type 2 AIH occurs most commonly in

children, typically under age 14, and it presents acutely with underlying cirrhosis being rare and is associated with other autoimmune diseases including autoimmune thyroiditis and type 1 diabetes mellitus. Anti-LKM1 antibody is positive in patients with type 2 AIH, but not in those with type 1 AIH in whom ANA, anti-SMA, and anti-SLA1 can be positive. Antimitochondrial antibody is a marker of primary biliary cholangitis, not AIH. Because type 2 AIH is generally seen in children, anti-LKM1 should not routinely be checked in adults presenting with suspicion for AIH. Notably, type 2 AIH generally presents more acutely (40% of patients) and has greater propensity to relapse after steroid withdrawal than type 1 AIH.

REFERENCE

Mack CL, Adams D, Assis DN, et al. Diagnosis and Management of Autoimmune Hepatitis in Adults and Children: 2019 Practice Guidance and Guidelines From the American Association for the Study of Liver Diseases. *Hepatology*. 2020;72(2):671-722. doi:10.1002/hep.31065

Question 42

A 21-year-old woman is diagnosed with autoimmune hepatitis and is prescribed prednisone and azathioprine. Within a week, she develops mid-abdominal pain, radiating to the back, and her lipase level is 537 U/L (reference range, 10-140 U/L).

What other medication may be useful in the treatment of this patient?

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.0	3.5-5.5
Alkaline phosphatase, serum, U/L	95	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	810	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	703	10-40
Bilirubin (total), serum, mg/dL	3.8	0.3-1.0
Hemoglobin, blood, g/dL	11.1	12-16
International normalized ratio	1.2	<1.1
Leukocyte count, cells/ μ L	11,100	4000-11,000
Platelet count, plts/ μ L	120,000	150,000-450,000
Protein (total), serum, g/dL	8.1	5.5-9.0

- A. Anakinra
- B. Cyclophosphamide
- C. Infliximab
- D. Mycophenolate mofetil
- E. Natalizumab

CORRECT ANSWER: D

RATIONALE

The 2 standard treatment regimens for autoimmune hepatitis include corticosteroids (prednisone or prednisolone) alone, or corticosteroids combined with azathioprine. The combination regimen allows for a lower dose of steroids and a lower incidence of side effects with the same therapeutic efficacy. This patient appears to have developed azathioprine-induced pancreatitis, which is a rare complication, more often seen in patients with Crohn’s disease who are treated with azathioprine. In patients who are intolerant of azathioprine (or who fail to respond to therapy), mycophenolate mofetil and calcineurin inhibitors (such as cyclosporin) have been used with success. There is data supporting the use of budesonide in place of prednisone, but this regimen is not as effective in patients with cirrhosis or advanced fibrosis, so it is reserved for patients with lesser degrees of liver fibrosis. The tumor necrosis factor alpha inhibitors are not used to treat autoimmune hepatitis, nor is the IL-1 inhibitor anakinra.

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Question 43

A 23-year-old woman with cystic fibrosis (CF; F508del mutation homozygote) presents with variceal hemorrhage. Her CF has been complicated by recurrent pulmonary infections, meconium ileus, and CF-related liver disease (CFLD) for which she was started on ursodiol at age 7.

Laboratory results reveal the following shown below.

Right upper quadrant ultrasound revealed a normal gall bladder, common bile duct of 3 mm, and an enlarged echogenic liver with nodular contour and splenomegaly. Doppler study showed normal flow in the hepatic and portal veins.

Which of the following patient factors has been associated with a lower risk of severe CFLD?

- A. Age >18
- B. F508del mutation homozygote
- C. Female
- D. History of meconium ileus
- E. Ursodiol

CORRECT ANSWER: C

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.0	3.5-5.5
Alkaline phosphatase, serum, U/L	105	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	110	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	97	10-40
Bilirubin (total), serum, mg/dL	2.1	0.3-1.0
Gamma-glutamyltransferase (GGT), serum, U/L	375	8-40
Hemoglobin, blood, g/dL	9.8	12-16
International normalized ratio	1.3	<1.1
Leukocyte count, cells/ μ L	9100	4000-11,000
Platelet count, pLts/ μ L	110,000	150,000-450,000

RATIONALE

Patients with CF frequently experience hepatobiliary complications (32% of patients by age 25), ranging from asymptomatic liver function test elevations (primarily AST, ALT, and GGT) to cirrhosis and portal hypertension, which occurs in approximately 5% to 10% of cases. A small number of children with CF experience neonatal cholestasis, with significant conjugated hyperbilirubinemia, while others experience a gradual progression to cirrhosis by late childhood. The pathogenesis of liver disease is thought to be due to the production of thick biliary secretions, similar to the thick mucus and pancreatic secretions caused by the *CFTR* mutation, which obstruct the biliary tree and induce inflammation and fibrosis. The diagnostic criteria for CFLD include hepatomegaly and/or splenomegaly, abnormal AST/ALT/GGT, ultrasound evidence of cirrhosis, or biopsy-proven biliary cirrhosis: if any 2 of these are present, the diagnosis of CFLD is made. Hepatic steatosis is common and can affect up to 60% of patients with CFLD. Ursodiol has historically been used to treat CFLD though its efficacy remains unclear. In the largest clinical series to date from France, 3328 patients with CF were followed and the incidence and predictors of severe CFLD were studied. Severe CFLD was rarely seen before age 5 with incidence of 10% of patients at age 30. Male sex, history of meconium ileus, and F508del mutation homozygotes was associated with increased risk of severe CFLD. Importantly, earlier adoption of ursodiol as was the case in this patient did not impact severity of CFLD.

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Question 44

An 18-year-old man with history of glycogen storage disease (type 1) is transitioning care to an adult hepatology clinic. His metabolic disease has

remained well controlled without symptomatic hypoglycemia. Even with control of his metabolic derangement, which long-term sequela may be expected in this patient?

- A. Cirrhosis
- B. Episodic hyperbilirubinemia
- C. Hepatocellular carcinoma
- D. Insulinoma
- E. Movement disorders

CORRECT ANSWER: C

RATIONALE

Glycogen storage disease type 1 (von Gierke disease) is an inborn error of metabolism occurring in 1 of 100,000 births. A defect in glucose-6-phosphatase makes it impossible for the child to break glycogen down into glucose. The glycogen-rich liver becomes enlarged, and the lack of glucose production leads to profound hypoglycemia and lactic acidosis between feedings, manifesting as lethargy and seizures. Patients also have significant hyperlipidemia and may develop xanthomata. Dietary management (frequent feedings either orally or via gastrostomy tube) can manage the hypoglycemia, but patients remain at risk for the development of hepatic adenomas, which may undergo malignant transformation in up to 10 percent of cases. Accordingly, screening for hepatocellular adenomas with ultrasound or computed tomography is routinely recommended. Liver transplantation may be considered when hepatocellular carcinoma is identified and leads to correction of much of the metabolic defect in this condition.

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Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	4.0	3.5-5.5
Alkaline phosphatase, serum, U/L	95	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	33	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	31	10-40
Bilirubin (total), serum, mg/dL	0.8	0.3-1.0
Hemoglobin, blood, g/dL	9.1	14-18
International normalized ratio	0.9	<1.1
Leukocyte count, cells/ μ L	9100	4000-11,000
Platelet count, plts/ μ L	95,000	150,000-450,000

Question 45

A 13-year-old boy of Eastern European descent, with a history of humeral and femoral fractures in the past, is found to have significant hepatosplenomegaly on physical examination.

Laboratory tests reveal the following results shown above.

Right upper quadrant ultrasound revealed a normal gallbladder, common bile duct of 3 mm, markedly enlarged liver and spleen with no liver masses noted. Doppler study showed normal flow in the hepatic and portal veins.

Which of the following enzyme deficiencies may be responsible for this clinical syndrome?

- A. Glucose 6-phosphate dehydrogenase
- B. Glucocerebrosidase
- C. Glycogen phosphorylase
- D. Hexosaminidase A
- E. Sphingomyelinase

CORRECT ANSWER: B

RATIONALE

Gaucher disease (GD) is a lysosomal storage disease caused by mutations in the beta-glucocerebrosidase gene, which leads to accumulation of glucocerebroside in macrophages, with the liver, spleen, and bone marrow being the major sites of accumulation. This is an autosomal recessive disorder that has a high prevalence in Ashkenazi Jewish populations. Clinical manifestations

typically include hepatosplenomegaly, and liver enzymes may be normal or only mildly elevated. On liver biopsy, Gaucher cells (lipid-laden macrophages) are prominent, with variable amounts of associated inflammation. Progression to cirrhosis and end-stage liver disease is rare, but patients with GD have an increased risk of hepatocellular carcinoma (as well as hematologic malignancies). Treatment of GD with drugs such as eliglustat will lead to a marked decrease in liver and spleen size.

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Question 46

A 43-year-old man undergoes liver transplantation for cirrhosis due to primary sclerosing cholangitis. His donor was positive for cytomegalovirus. His surgery is uncomplicated, with peak laboratory test results following reperfusion noted in the table shown at the top of the following page. He has conventional arterial anatomy with a choledochocholedochostomy (duct-to-duct) biliary anastomosis.

On day 1 after his operation, his liver enzymes rise dramatically to peak, as noted in the table shown at the top of the following page.

A liver ultrasound with dopplers reveals no flow through his hepatic artery. He returns to the operating room for surgical thrombectomy and hepatic artery reconstruction.

Laboratory Test	Initial Result	Day 1 Postoperation Result	Reference Range
Alkaline phosphatase, serum, U/L	183	230	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	233	3479	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	176	2876	10-40
Bilirubin (total), serum, mg/dL	3.0	4.5	0.3-1.0

Which of the following is most likely to be long-term sequelae from this ischemic injury?

- A. Biliary anastomotic stricture
- B. Biliary nonanastomotic stricture
- C. Hepatic fibrosis
- D. Portal hypertension

CORRECT ANSWER: B

RATIONALE

The liver receives 70% of its blood supply from the portal vein and 30% from the hepatic artery, though bile ducts are disproportionately dependent upon arterial blood supply and therefore particularly susceptible to arterial ischemic injury. Ischemic cholangiopathy is a rare condition of bile duct injury due to impaired blood supply. It is most commonly associated with liver transplantation and with the administration of hepatic intra-arterial chemotherapy, but it is also seen in AIDS cholangiopathy, polyarteritis nodosa, and hereditary hemorrhagic telangiectasia. Clinical features can range from asymptomatic liver enzyme abnormalities (mainly alkaline phosphatase and gamma-glutamyltransferase) to progressive cholestasis with jaundice. Ischemic stenosis of the common bile duct can also present as acute obstructive jaundice or cholangitis, though more commonly, this global arterial ischemia results in the finding of diffuse biliary strictures. Although anastomotic strictures can occur, these are rarely in isolation if there has been a significant arterial ischemia event. Despite significant rise in transaminases, acute hepatic necrosis is rare in hepatic artery thrombosis and in general, ischemic injury to the liver, whether from thrombosis or low flow states, leads to a rapid rise and fall of transaminases with no chronic hepatocyte injury consequent to the transient ischemia.

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Question 47

A 34-year-old woman undergoes a hematopoietic stem cell transplant (HSCT) for acute myeloid leukemia. She receives myeloablative-conditioning therapy with busulfan and cyclophosphamide. On day 15 after HSCT, she develops jaundice, right upper quadrant pain, and ascites. She undergoes transjugular liver biopsy with normal hepatic vein venogram and hepatic venous pressure gradient of 18 mmHg. Histology reveals congestion in zone 3 with associated hemorrhage and collagen deposition within the central vein.

What is the best treatment for this patient?

- A. Defibrotide
- B. Intravenous heparin
- C. Liver transplantation
- D. Thrombolysis
- E. Transjugular intrahepatic portosystemic shunt

CORRECT ANSWER: A

RATIONALE

This patient presents with classic symptoms of sinusoidal obstruction syndrome (SOS) following high-intensity myeloablative-conditioning therapy

for HSCT. Busulfan and cyclophosphamide are both associated with higher risk of SOS compared with lower intensity, nonmyeloablative-conditioning regimens. SOS develops within the first month after HSCT, and in the case of cyclophosphamide conditioning, typically within 20 days. This patient meets diagnostic clinical criteria based on Seattle Criteria (at least 2 of following criteria within 20 days of HSCT: total bilirubin >2 mg/dL, hepatomegaly or right upper quadrant pain, >2% weight gain). In addition, hepatic venous pressure gradient (HVPG) more than 10 mmHg is highly specific for SOS (91%) and histology is consistent showing classic early findings of zone 3 congestion and early collagen deposition that subsequently progresses to nonthrombotic occlusion of central veins and sinusoids. Aside from diuretic therapy, treatment options are limited. Anticoagulation alone or in conjunction with thrombolysis has been studied with high rates of bleeding and little clinical benefit (29% survival) and is not recommended. Transjugular intrahepatic portosystemic shunt (TIPS) is effective for treating portal hypertension (mean reduction in HVPG from 20.2 mmHg to 6.4 mmHg) but does not improve survival (3-month mortality, 87.5%) and is not recommended for severe SOS after HSCT. There is limited evidence to support TIPS in SOS following solid organ transplant. Liver transplantation for SOS can be considered in patients with benign conditions or malignancy with favorable prognosis but would not be considered in this patient having just undergone therapy for acute myelogenous leukemia. Defibrotide is a single-stranded polydeoxyribonucleic acid with fibrinolytic, antithrombotic, and antiischemic properties. Defibrotide (6.25 mg/kg) given for at least 14 days led to complete remission in up to 55% of patients and survival past day 100 after HSCT of 43%, both significantly improved compared with historical controls. The US Food and Drug Administration approved defibrotide for the treatment of severe SOS in April 2016. There is also data to support defibrotide for prophylaxis of HSCT though this is currently limited to the pediatric population.

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Question 48

A 27-year-old man with a history of bipolar disorder presents to the emergency department with jaundice. His vital signs are as follows: heart rate, 100 bpm and regular; blood pressure, 125/70 mmHg; respiratory rate, 14 breaths per minute; oxygen saturation, 98% on room air. His examination is remarkable for jaundice and moderate right upper quadrant (RUQ) tenderness on palpation.

Laboratory tests reveal results shown at the top on the following page.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.9	3.5–5.5
Alkaline phosphatase, serum, U/L	43	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	555	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	650	10–40
Bilirubin, serum Total, mg/dL	4.1	0.3–1.0
Direct, mg/dL	0.6	0.1–0.3
Creatinine, serum, mg/dL	2.1	0.7–1.5
Hemoglobin, blood, g/dL	8.5	14–18
International normalized ratio	1.7	<1.1
Leukocyte count, cells/ μ L	9100	4000–11,000
Mean corpuscular volume, fL	103	80–98
Platelet count, plts/ μ L	120,000	150,000–450,000

RUQ ultrasound revealed a normal gall bladder with no gallstones, common bile duct was 3 mm, liver was of normal size and contour but with steatosis present, no liver masses were seen, Doppler study showed normal flow in the hepatic and portal veins. Reticulocyte count is 24 percent, haptoglobin is lower than 6 mg/dL, lactate dehydrogenase is significantly elevated, and peripheral smear shows no schistocytes, but macrocytes and nucleated red blood cells.

What is the most appropriate treatment for this patient?

- A. Corticosteroids
- B. D-penicillamine
- C. Liver transplantation
- D. Trientine
- E. Zinc

CORRECT ANSWER: C

RATIONALE

This is a case of acute Wilsonian hepatitis. Clinical clues include the marked transaminitis and evidence of liver failure with a low alkaline phosphatase level, and a Coombs negative hemolytic anemia due to copper-induced lysis of red blood cells. The patient's psychiatric history is also suggestive, as many patients with Wilson's disease have a history of neuro-psychiatric disorders, including Parkinsonian movement disorders and

psychotic disorders. Wilson's disease is uniformly fatal without treatment and patients such as this with severe acute presentation, liver transplantation should be pursued. Trientine and D-penicillamine are both copper chelating agents, though these are reserved for treatment of subacute or chronic disease with trientine being favored due to its favorable side effect profile. Zinc can impair copper absorption in the gut and is effective for maintenance therapy in patients with chronic Wilson's disease in whom chelating therapy has depleted excess copper. Corticosteroids have no role in the treatment of Wilson's disease.

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Question 49

A 19-year-old woman with history of schizoaffective disorder presents with fatigue and jaundice.

Initial liver enzymes reveal results that are shown at the top of the following page.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.0	3.5-5.5
Alkaline phosphatase, serum, U/L	57	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	305	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	292	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0
International normalized ratio	1.2	<1.1

Complete blood count is unremarkable with normal platelet count. Right upper quadrant ultrasound revealed a normal gall bladder with no gallstones, common bile duct was 3 mm, liver was of small size with a nodular contour, no liver masses were seen, Doppler study showed normal flow in the hepatic and portal veins. Ophthalmologic examination shows no Kayser-Fleischer rings. A liver biopsy is performed and shows lymphoplasmacytic portal infiltrate with interface hepatitis and patchy rhodamine blue staining.

Which of the following tests is consistent with this patient’s diagnosis?

- A. Anti-nuclear antibody titer higher than 1:320
- B. Positive smooth muscle antibody
- C. Serum ceruloplasmin level of 60 mg/L
- D. Serum non-ceruloplasmin-bound copper level lower than 150 µg/L
- E. Urine copper level of 180 µg/24 hours

CORRECT ANSWER: E

RATIONALE

Wilson’s disease (WD) is caused by a mutation in the P-type ATP-ase that mediates the excretion of copper into the bile. Failure to excrete copper leads to deposition in the liver, eyes, and brain. Hepatic involvement can manifest as chronic progressive liver injury leading to cirrhosis, and an acute fulminant hepatitis that is treatable only with transplantation. Neurologic symptoms are due to deposition in the basal ganglia and other brain structures and include Parkinsonian symptoms, dysautonomia, and behavioral changes. The diagnosis of WD is made via several biochemical tests. Serum ceruloplasmin levels lower than 20

mg/dL warrants further workup for WD, while a level lower than 5 mg/dL is highly suggestive, though this can be falsely elevated in patients with acute hepatitis given that ceruloplasmin is an acute phase reactant. Urine copper levels higher than 100 µg/24 hours are highly suggestive, while levels higher than 40 µg/24 hours period warrant additional testing. Notably, elevated urine copper in this indeterminate range (40-100 µg/24 hours) can be seen in severe hepatic injury of any cause. Serum copper levels are often decreased due to the decrease in circulating ceruloplasmin, which is the major copper-binding protein in serum. However, non-ceruloplasmin-bound copper will be elevated, typically above 250 µg/L. Kayser-Fleischer rings, when present, are a strong indicator of WD in a patient with a low serum ceruloplasmin. However, this finding is seen in only 44% to 62% of cases of isolated hepatic disease, while it is almost always present in patients with neurologic WD. Liver biopsy may also be used to diagnose WD, with a hepatic copper content higher than 250 µg/g highly suggestive of this diagnosis. Rhodamine blue stain, which is specific for copper deposition in hepatocytes can provide qualitative data to support hepatic copper overload, though this is often patchy. Notably, liver biopsy in WD has no characteristic features with steatohepatitis and autoimmune-like pictures being described.

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Palumbo CS, Schilsky ML. Clinical practice guidelines in Wilson disease. *Ann of Transl Med*. 2019;7(S2):S65-S65. doi:10.21037/atm.2018.12.53

Question 50

A 19-year-old man with elevated liver enzymes is found to have a serum ceruloplasmin of 3 mg/dL (reference range, 25–43 mg/dL), non-ceruloplasmin-bound copper of 36 µg/dL, and a urine copper excretion of 210 µg/24 hours (reference range, 0–100 µg/24 hr). He is prescribed trientine to treat his illness.

Which of the following laboratory changes would you expect to see after 6 months of therapy?

- A. Increase in non-ceruloplasmin-bound copper
- B. Decrease in urine copper excretion compared with baseline
- C. Increase in urine copper excretion compared with baseline
- D. No urine copper should be found if therapy is effective
- E. No change in non-ceruloplasmin-bound copper

CORRECT ANSWER: C**RATIONALE**

A serum ceruloplasmin less than 5 mg/L and a 24-hour urine copper excretion greater than 100 µg/24 hours are both highly suggestive of Wilson's disease, a disorder of copper metabolism caused by a mutation in a P-type ATP-ase (encoded by *ATP7B*) that mediates the excretion of copper into the bile. Treatment of Wilson's disease consists of copper chelation therapy. Commonly used therapies include D-penicillamine, trientine, and zinc. Patients on therapy should have 24-hour urine copper determination every 6 to 12 months. Initial urine copper excretion will increase up to 1000 µg/24 hours with subsequent decrease with effective chelation of copper and excretion. Patients receiving maintenance trientine or D-penicillamine should have urine copper excretion of 200 to 500 µg/24 hours. Patients can be considered for zinc therapy if urinary copper excretion falls below 150 µg/24 hours with goal copper excretion in the range of 75 µg/24 hours. Non-ceruloplasmin-bound copper will decrease with effective chela-

tion therapy, ideally to a goal level lower than 10 µg/dL, with levels above this suggestive of ineffective chelation based on dose or noncompliance.

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CHAPTER 7

Cirrhosis and liver transplantation

Matthew Stotts, MD and Kathleen Viveiros, MD

Question 1

A 51-year-old woman with compensated hepatitis C virus (HCV)-related cirrhosis presents for evaluation. She had previously been treated for HCV and was diagnosed with cirrhosis on a biopsy at that time. She does not drink alcohol and has no other risk factors for liver disease. Her blood tests are notable for a normal bilirubin, albumin, international normalized ratio, creatinine, and liver enzymes. Her platelet count is 120,000/ μ L and her HCV viral load is negative. Transient elastography is performed and shows a liver stiffness measurement of 21.1 kPa.

Which of the following is the best option regarding primary prophylaxis of variceal hemorrhage in this patient?

- A. She is at low risk of variceal bleeding and should not undergo an endoscopy at this time
- B. She should undergo an upper endoscopy to screen for varices; if none are present and she remains clinically stable, she should have a repeat upper endoscopy in 1-2 years
- C. She should undergo an upper endoscopy to screen for varices; if none are present and she remains clinically stable, she should have a repeat upper endoscopy in 3 years
- D. She should undergo an upper endoscopy to screen for varices; if none are present, she should be started on a nonselective beta-blocker and have a repeat endoscopy in 1-2 years

CORRECT ANSWER: C**RATIONALE**

Upper endoscopy should be performed in any patient with cirrhosis to screen for varices, with the exception of those with compensated cirrhosis, a platelet count above 150,000 platelets/ μ L, and a liver stiffness measurement below 20 kPa. If no varices are found in a patient with compensated cirrhosis, recommendations are for a screening endoscopy to be repeated every 2 years in those with ongoing liver injury and every 3 years in those without ongoing liver injury. Given that she has no risk factors for ongoing liver injury (such as alcohol use, obesity, or untreated viral hepatitis), she should have a repeat endoscopy in 3 years.

Answer (A) is incorrect because her thrombocytopenia and liver stiffness measurements place her at risk for the presence of high-risk varices. Answer (B) is incorrect because she does not need a repeat endoscopy so soon. If she was found to have small varices and was not started on a nonselective beta-blocker (NSBB), a repeat endoscopy would be recommended in 1 to 2 years. If she had ongoing liver injury (such as ongoing alcohol use or active HCV infection), a repeat endoscopy would be recommended in 2 years. Answer (D) is incorrect because there is currently no evidence to recommend using NSBBs to prevent the formation of varices in this patient. In addition, in individuals with varices that have not bled, endoscopy does not need to be repeated in patients who are taking NSBBs.

REFERENCE

Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology*. 2017;65(1):310-335. doi:10.1002/hep.28906

Question 2

A 48-year-old man with compensated cirrhosis secondary to hepatitis B is diagnosed with a hepatocellular carcinoma (HCC). He has an excellent functional status and no other major medical comorbidities. His only medications include entecavir for management of his hepatitis B and twice-daily carvedilol for large varices that have not bled. His blood tests show normal liver tests, chronic thrombocytopenia (platelets 60,000/ μ L), and an alpha fetoprotein that is elevated at 32 ng/mL. His blood tests and laboratory values are consistent with a MELD (Model for End-Stage Liver Disease) score of 7 and Child-Pugh class A cirrhosis. Multiphasic computed tomography (CT) imaging of his liver and noncontrast CT imaging of his lungs shows a 4.2 cm HCC in the left lobe (segment 4) of his liver without vascular invasion or evidence of metastatic disease.

Which of the following is the most appropriate next step in the treatment of his HCC?

- A. Surgical resection of his liver mass
- B. Referral for liver transplantation
- C. Transarterial chemoembolization and systemic therapy
- D. Systemic therapy and transition to supportive care if his disease progresses on systemic therapy

CORRECT ANSWER: B

RATIONALE

This patient should be referred for liver transplantation, as he is within Milan criteria (single mass <5 cm or up to 3 masses <3 cm each, in the absence

of vascular invasion or metastatic disease). Liver transplantation will provide him his best chance for long-term survival. While awaiting transplantation, he can undergo locoregional therapies to control his tumor burden. Answer (A) is incorrect because his underlying clinically significant portal hypertension (as evidenced by his large esophageal varices, thrombocytopenia, and splenomegaly) make him a poor resection candidate. Answer (C) and (D) are incorrect as this patient is a candidate for a curative therapy (liver transplantation).

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Heimbach JK, Kulik LM, Finn RS, et al. AASLD guidelines for the treatment of hepatocellular carcinoma. *Hepatology*. 2018;67(1):358-380. doi:10.1002/hep.29086

Question 3

A 44-year-old woman undergoes liver transplantation in the setting of decompensated cirrhosis from autoimmune hepatitis (AIH).

Which of the following is the most accurate regarding her risk of recurrent AIH after liver transplantation?

- A. Liver transplantation is curative of this disease, with little or no chance of recurrence in those who are compliant with immunosuppressant therapy
- B. Most patients with recurrent AIH fail to respond to intensified immunosuppressive therapy
- C. Patients with AIH usually require higher doses of baseline immunosuppression after transplantation
- D. The majority of patients who undergo transplantation for AIH will have recurrent autoimmune liver disease after transplantation

CORRECT ANSWER: C**RATIONALE**

Individuals with AIH have an approximately 20% chance of recurrent disease after transplantation. This risk is higher if immunosuppression is rapidly tapered after transplantation, and most centers manage patients with a higher baseline level of immunosuppression compared with recipients with other etiologies of liver disease. Recurrent AIH will typically respond to increasing basal immunosuppression. Answers (A) and (B) are incorrect since around one-fifth of patients will have recurrent disease after transplantation. Answer (D) is incorrect because recurrent disease will usually respond to appropriate medical management.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

González-Koch A, Czaja AJ, Carpenter HA, et al. Recurrent autoimmune hepatitis after orthotopic liver transplantation. *Liver Transpl*. 2001;7(4):302-310. doi:10.1053/jlts.2001.21449

Question 4

A 62-year-old man undergoes transplantation evaluation in the setting of newly diagnosed decompensated cirrhosis. He is diagnosed with hepatitis C virus (HCV) with active viremia. He is otherwise felt to be a good medical candidate for liver transplantation, with a Model for End-Stage Liver Disease (MELD)-Na score of 20.

Which of the following is the most accurate statement regarding the treatment of HCV for this patient?

A. Defer HCV treatment before transplantation, as HCV can be cured with transplantation with the need for expensive regimens

- B. Defer HCV treatment as it may not significantly improve the patient's health but could result in clinical improvement that would limit his access to transplantation
- C. Treat HCV before transplantation to avoid drug-drug interactions between direct-acting antivirals and immunosuppressant medications
- D. Treat HCV after transplantation as this would allow the patient to be eligible for HCV-positive organs

CORRECT ANSWER: B**RATIONALE**

All patients with HCV infection should be considered for therapy, given the tolerability and efficacy of direct-acting antiviral therapies. In those awaiting transplantation, however, treatment decisions need to be made on a case-by-case basis, as there are a variety of potential risks and benefits with each treatment strategy. Potential benefits of treatment before transplantation include stabilizing or improving liver function before surgery and preventing liver graft infection at transplantation. Potential risks of treatment before transplantation include having higher rates of treatment failure with decompensated liver disease and that successful treatment may leave patients with a diseased liver but improve their MELD score enough to limit access to organs (often referred to as “MELD purgatory”). Answer (A) is incorrect because HCV can easily be treated with a variety of DAAs after transplantation. Answer (D) is incorrect because individuals who are not viremic for HCV can still be considered for transplantation with HCV-positive organs. Answer (C) is incorrect as HCV will universally infect the liver graft in any individual with active HCV at the time of transplantation.

REFERENCE

Belli LS, Berenguer M, Cortesi PA, et al. Delisting of liver transplant candidates with chronic hepatitis C after viral eradication: A European study. *J Hepatol*. 2016;65(3):524-531. doi:10.1016/j.jhep.2016.05.010

Question 5

A 50-year-old man with cirrhosis secondary to chronic hepatitis B and alcohol develops significant hypoxia and dyspnea over months, now requiring 6 liters of home oxygen therapy. His prior decompensations include ascites controlled on medications and a remote history of variceal bleeding. His evaluation has included a normal chest radiograph, a negative computed tomography of his chest without evidence of pulmonary embolism, and an echocardiogram showing evidence of a small patent foramen ovale and microbubbles seen in the left atrium 5 cardiac cycles after appearing in the right atrium.

Which of the following is the most accurate statement in the diagnosis or treatment of this patient?

- A. An arterial blood gas showing a partial pressure of oxygen (PaO₂) lower than 60 mmHg on room air would be an indication to list him for transplantation with exception points.
- B. Liver transplantation should be considered immediately as his condition would likely resolve within days of transplantation.
- C. Liver transplantation should be considered if he fails medical therapy with octreotide, nitric oxide synthase inhibitors, methylene blue, or placement of a transjugular intrahepatic portosystemic shunt (TIPS)
- D. Pulmonary function testing would reveal normal spirometry, lung volumes, and diffusing capacity of carbon monoxide (DLCO)

CORRECT ANSWER: A

RATIONALE

This patient has hepatopulmonary syndrome based off the presence of underlying liver disease, impaired oxygenation, and evidence of intrapulmonary vascular shunting. When present, an arterial blood gas should be obtained with the expectation of an elevated alveolar-arterial gradient and a reduced PaO₂. If his disease is graded as severe

(with a PaO₂ <60 mmHg on room air), he will be a candidate for liver transplantation and can expect gradual improvement in his hypoxia over the next 6 to 12 months.

DLCO is usually mildly to severely impaired in hepatopulmonary syndrome. Response to medical therapies is overall ineffective and response to transjugular intrahepatic portosystemic shunt has been reported with variable results and is not generally recommended. Recovery from hepatopulmonary syndrome can be delayed for up to 1 year after transplantation.

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Rodríguez-Roisin R, Krowka MJ. Hepatopulmonary syndrome--a liver-induced lung vascular disorder. *N Engl J Med.* 2008;358(22):2378-2387. doi:10.1056/NEJMra0707185

Question 6

A 53-year-old woman with decompensated cirrhosis secondary to alcohol complains of spontaneous muscle cramps that intermittently occur at night and significantly affect her quality of life. On multiple occasions, she has undergone testing that has revealed normal electrolytes (including potassium and magnesium), and she has not had any evidence of zinc deficiency on examination or on serum blood tests.

Which of the following is the most accurate regarding this patient's symptoms?

- A. They are likely related to her liver disease and muscle cramps can be improved with multiple different supplements
- B. They are likely related to her liver disease, but no therapies have been shown to be effective

- C. They are not related to her liver disease and should pursue management through her primary care provider
- D. They suggest ongoing alcohol use and should lead to discussions about ongoing alcohol use

CORRECT ANSWER: A

RATIONALE

Muscle cramps are commonly seen with cirrhosis. In general, correcting deficiencies in zinc, potassium, and magnesium are low-risk interventions that should be performed in anyone with deficiencies. A variety of preliminary data supports the use of agents such as baclofen, vitamin E, and taurine. Because muscle cramps are commonly seen in those with cirrhosis, answers (A) and (D) are incorrect. Answer (B) is incorrect as several therapies have been shown to have potential benefit.

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Henry ZH, Northup PG. Baclofen for the treatment of muscle cramps in patients with cirrhosis: A new alternative. *Hepatology*. 2016;64(2):695-696. doi:10.1002/hep.27988

Vidot H, Cvejic E, Carey S, et al. Randomised clinical trial: oral taurine supplementation versus placebo reduces muscle cramps in patients with chronic liver disease. *Aliment Pharmacol Ther*. 2018;48(7):704-712. doi:10.1111/apt.14950

Question 7

A 40-year-old man with alcohol-related cirrhosis

presents with large-volume hematemesis, presumed related to an acute variceal bleed. He is intubated on arrival for concerns regarding his airway protection. On examination, he is intubated and sedated with scleral icterus and multiple spider angiomas. He remains tachycardic. Laboratory tests show a hemoglobin of 6.1 g/dL (reference range [male], 14-18 g/dL), platelet count of 71,000 plts/ μ L (reference range, 150,000–450,000 plts/ μ L), and an elevated lactic acid.

Which of the following is the most accurate regarding the initial management of this patient?

- A. He should undergo a blood transfusion with a goal hemoglobin >10 g/dL
- B. He should be started on a proton pump inhibitor
- C. He should be started on prophylactic antibiotics
- D. He should undergo endoscopic sclerotherapy within 12 hours of presentation

CORRECT ANSWER: C

RATIONALE

This patient is at high risk of infection, and prophylactic antibiotics have been shown to improve a variety of clinical outcomes, including reduced rates of bacterial infections, rebleeding, and death. A more restrictive transfusion strategy (targeting a hemoglobin of 7-9 g/dL and transfusing when hemoglobin fell below 7 g/dL) was shown to improve survival in a randomized controlled trial that included individuals with cirrhosis. Although proton pump inhibitors are often started at presentation, it is more important to start a vasoconstrictor like octreotide. Sclerotherapy has been associated with more side effects than endoscopic variceal ligation.

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Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology*. 2017;65(1):310-335. doi:10.1002/hep.28906

Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med*. 2013;368(1):11-21. doi:10.1056/NEJMoa1211801

Villanueva C, Piqueras M, Aracil C, et al. A randomized controlled trial comparing ligation and sclerotherapy as emergency endoscopic treatment added to somatostatin in acute variceal bleeding. *J Hepatol*. 2006;45(4):560-567. doi:10.1016/j.jhep.2006.05.016

Question 8

A 22-year-old man develops acute liver injury in the setting of an intentional overdose of acetaminophen 2 days before presentation. He is evaluated by the transplantation team, including psychiatry, and felt to be an acceptable transplantation candidate. Despite medical management including N-acetylcysteine, he develops progressive encephalopathy requiring intubation and his laboratory test results are notable for persistent international normalized ratio higher than 10 (reference range, <1.1) and ammonia levels persistently higher than 200 µg/dL (reference range, 40-70 µg/dL). It is felt that he is unlikely to survive the following week without transplantation.

Which of the following clinical situations, if present, would preclude transplantation?

- A. Any evidence of a bacterial infection
- B. Any prior history of suicidal attempts or suicidal ideations prior to presentation
- C. Evidence of hemodynamic instability requiring use of inotrope medications
- D. The presence of fixed and fully dilated pupils on examination

CORRECT ANSWER: D

RATIONALE

This patient has acute liver failure with an expected survival of only days, and he can be listed immediately for transplantation as a “status 1a” patient, meaning he would have preference for

transplantation over all individuals listed with chronic liver disease. One of the most feared outcomes of transplantation, however, is failing to recover neurological function. Objective evidence of brainstem injury (with fixed and dilated pupils as described above) should preclude transplantation as it is likely to be futile.

Bacterial infection and psychiatric disease are relative contraindications but should not preclude transplantation. Bacterial infection can be managed with appropriate antibiotic therapy. The need for inotrope support is common with acute liver failure and can indicate disease severity (meaning the need to proceed with transplantation). Transplantation could potentially be futile if he has rapidly escalating inotrope requirements.

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- Martin P, DiMartini A, Feng S, Brown R Jr, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Hepatology*. 2014;59(3):1144-1165. doi:10.1002/hep.26972

Question 9

Which of the following patients is the most reasonable candidate for preemptive (“early”) transjugular intrahepatic portosystemic shunt (TIPS) placement for esophageal varices?

- A. 55-year-old with compensated cirrhosis (Child-Pugh class A) who presents with hematemesis and is found to have evidence of recent variceal bleeding on endoscopy, successfully treated with band ligation
- B. 63-year-old with decompensated cirrhosis (Child-Pugh class C) who undergoes an

endoscopy for variceal screening and is found to have large esophageal varices

- C. 70-year-old with decompensated cirrhosis (Child-Pugh class B) who presents with hematemesis and is found to have active variceal bleeding on endoscopy that is successfully treated with band ligation
- D. 79-year-old with end-stage renal disease and decompensated cirrhosis (Child-Pugh class C) who presents with hematemesis and is found to have large varices with evidence of recent bleeding, successfully treated with band ligation

CORRECT ANSWER: C

RATIONALE

Several studies have suggested benefit with early TIPS for individuals who present with variceal hemorrhage. TIPS placement has associated costs and risks, and this therapy should be reserved for individuals who meet inclusion criteria of studies that have shown benefit. The population that is often referenced in this setting are those who present with a variceal hemorrhage and are Child-Pugh class C (score 10-13) or Child-Pugh class B (score 7-9) with active hemorrhage on endoscopy. Notably renal disease and age above 75 were exclusion criteria.

Patients who have not experienced a variceal bleed should follow recommendations for primary prophylaxis. Other choices are incorrect as these include patients who were not included in the aforementioned studies (due to age, renal failure, and Child-Pugh class A cirrhosis).

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ment: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology*. 2017;65(1):310-335. doi:10.1002/hep.28906

Question 10

A 61-year-old woman with compensated hepatitis C-related cirrhosis is found to have a 2.1 cm mass on a right upper quadrant ultrasound. She has had multiple images of her abdomen in the last 2 months related to abdominal pain, including a computed tomography (CT) scan of her abdomen with oral and intravenous contrast 7 weeks before and a noncontrast CT of her abdomen diagnosing her with kidney stones just last week. Neither of these images had any concerns for a liver mass. Her liver disease is compensated (Child-Pugh class A) and her liver tests all remain at baseline with a low Model for End-Stage Liver Disease (MELD) score. An alpha fetoprotein level is checked and normal at 2.3 ng/mL.

Which of the following should be recommended as a next best step in evaluation?

- A. No further testing is needed at this time, as she has had recent cross-sectional imaging. She should have an ultrasound in 6 months for ongoing hepatocellular carcinoma (HCC) screening
- B. She should undergo magnetic resonance imaging (MRI) without contrast given the discrepancy between the ultrasound and CT scans. If a mass is seen, she should undergo a biopsy
- C. She should undergo a multiphasic CT of her liver with intravenous contrast
- D. She should be scheduled for an ultrasound guided biopsy of this liver lesion with interventional radiology to rule out malignancy

CORRECT ANSWER: C

RATIONALE

Answer (C) is correct. This patient was found to

have a liver mass on ultrasound, which is highly concerning for HCC given her baseline cirrhosis. Diagnosis can often be made without biopsy, when dynamic imaging of the liver (either CT or MRI) reveals the typical features of HCC (arterial hypervascularity and early washout in the portal venous phase).

Her recent CT imaging is not adequate to evaluate for HCC as it was done without contrast. HCC would not be evident on noncontrast CT imaging of the liver and could easily be missed on a single-phase CT of her abdomen (which would have only obtained a venous phase). A biopsy would not be necessary if the lesion can be accurately diagnosed with typical imaging features.

REFERENCE

Heimbach JK, Kulik LM, Finn RS, et al. AASLD guidelines for the treatment of hepatocellular carcinoma. *Hepatology*. 2018;67(1):358-380. doi:10.1002/hep.29086

Question 11

A 55-year-old man with compensated cirrhosis secondary to nonalcoholic fatty liver disease presents to his primary care physician. He has had chronic low back pain and wants recommendations regarding pain management.

Which of the following is the most accurate regarding the use of analgesics in individuals with cirrhosis?

- A. Acetaminophen is considered safe in doses up to 4000 mg daily
- B. All systemic analgesics should be avoided. Local therapies, such as topical creams or patches, should be used
- C. Nonsteroidal antiinflammatory drugs should be considered first-line therapy
- D. Opioid medications should be avoided, due to the risk of adverse events

CORRECT ANSWER: D

RATIONALE

The management of chronic pain in individuals with cirrhosis can be challenging. When systemic medications are needed, acetaminophen is considered safe and is the recommended first-line pharmacologic therapy for pain in this population, at a dose of up to 2000 mg daily. Nonsteroidal antiinflammatory drugs should be avoided, as several studies have shown that these drugs increase the risk of renal injury, ascites, and bleeding in this population. Individuals with cirrhosis are among those with the highest risk of adverse events related to opioids. When required, careful attention must be paid to preventing constipation and encephalopathy and assessing risk factors for prescription drug abuse, with the goal of using the lowest effective dose for the shortest duration of time.

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Question 12

A 42-year-old man is hospitalized with jaundice and new-onset ascites and diagnosed with severe alcoholic hepatitis in the setting of heavy alcohol use with his last drink 3 weeks before admission. He has never had prior health consequences related to alcohol and no prior psychiatric or medical comorbidities. He and his wife verify no prior knowledge of liver disease. He has never

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	2.5	3.5–5.5
Bilirubin (total), serum, mg/dL	27.7	0.3–1.0
Creatinine, serum, mg/dL	0.8	0.7–1.5
International normalized ratio	2.5	<1.1

undergone alcohol counseling or rehabilitation but states he is “done with alcohol.” Laboratory test results are shown above.

His Model for End-Stage Liver Disease (MELD) score on admission is 30, and his Maddrey’s discriminant function is 72. It is elected to start him on a course of oral prednisolone and, after 7 days, his MELD score has risen to 34. A Lille score is calculated and consistent with nonresponse to medical therapy.

Which of the following is most appropriate next step in his management?

- A. He should continue prednisolone for a total of 28 days and be followed up clinically; he can expect gradual improvement in his jaundice over the course of months if he is able to maintain abstinence
- B. He should stop prednisolone and expect gradual improvement if he is able to maintain abstinence
- C. He should stop prednisolone and be referred to a tertiary center for considerations of early transplantation
- D. He has a very high short-term mortality and should undergo goals of care discussions

CORRECT ANSWER: C

RATIONALE

This patient has a high short-term mortality and should be considered for early liver transplantation. In a study published in the *New England Journal of Medicine* in 2011, individuals with severe alcoholic hepatitis that did not respond to glucocorticoid therapy were found to have a markedly improved 6-month survival (77% vs 23%) if they underwent early liver transplantation, com-

pared with controls who were matched according to age, sex, and disease severity. Notably, patients in this study were highly selected, including a requirement of close supportive family members, an absence of psychiatric disorders, a commitment to abstinence, and no prior liver-decompensating events. This patient may be an acceptable candidate for transplantation and should be referred for evaluation early. The patient has a high short-term mortality based off his Maddrey’s discriminant function and Lille score.

REFERENCE

Mathurin P, Moreno C, Samuel D, et al. Early liver transplantation for severe alcoholic hepatitis. *N Engl J Med*. 2011;365(19):1790–1800. doi:10.1056/NEJMoa1105703

Question 13

A 74-year-old woman is evaluated in transplantation clinic in the setting of decompensated cirrhosis with ascites, hepatic encephalopathy, and esophageal varices that have not bled. Before her recent diagnosis of liver disease, her only prior medical problems were hypertension and hyperlipidemia. She exercised regularly. Her evaluation is notable for a MELD (Model for End-Stage Liver Disease) score of 28, Child-Pugh class C, and blood group AB, without any significant concerns on her additional testing.

Which of the following is the most accurate regarding liver transplantation in this patient?

- A. Age above 70 is widely considered a contraindication to transplantation
- B. Transplantation should only be offered if she has an acceptable living donor candidate

- C. Transplant recipients in this age group have inferior overall outcomes compared with younger age groups
- D. Transplant recipients in this age group have overall outcomes that are similar with those in younger age groups

CORRECT ANSWER: C

RATIONALE

It is generally accepted that physiological, not chronological, age should determine who is a candidate for liver transplantation. Older patients can be listed for liver transplantation after careful considerations of their comorbidities and functional status. Although carefully selected patients have acceptable overall outcomes, these outcomes are inferior to those in younger age groups.

Patients should only be considered candidates for living donation if they are also candidate for deceased donation, and her liver disease is advanced enough that she could have access to a deceased donor organ given her blood group.

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Aduen JF, Sujay B, Dickson RC, et al. Outcomes after liver transplant in patients aged 70 years or older compared with those younger than 60 years. *Mayo Clin Proc.* 2009;84(11):973-978. doi:10.1016/S0025-6196(11)60667-8

Lipshutz GS, Hiatt J, Ghobrial RM, et al. Outcome of liver transplantation in septuagenarians: a single-center experience. *Arch Surg.* 2007;142(8):775-784. doi:10.1001/archsurg.142.8.775

Question 14

A 48-year-old man with decompensated cirrhosis secondary to nonalcoholic fatty liver disease (NASH) and chronic kidney disease (baseline creatinine, 1.5 mg/dL; glomerular filtration rate (GFR), 55 mL/min) is seen in clinic. His Model

for End-Stage Liver Disease (MELD) laboratory test results have progressively worsened, and it is expected that he will likely be getting organ offers in the near future. His worsening MELD was driven in part by worsening renal function and a creatinine that is now 2.0 mg/dL (GFR of 40 mL/min).

Which of the following statements is the most accurate regarding this patient's options for renal transplantation?

- A. Normalization of his kidney function after liver transplantation and avoid renal transplantation
- B. Worsening renal function after liver transplantation and should be considered for simultaneous liver and kidney transplantation
- C. If kidney disease worsens after liver transplantation, the patient can be listed for renal transplantation
- D. If kidney disease worsens after liver transplantation, the patient can be listed for kidney transplantation and will be prioritized on the list

CORRECT ANSWER: D

RATIONALE

This patient has underlying chronic kidney disease which may very likely worsen after transplantation related to the acute stressors of surgery and side effects of medications he will likely receive. In 2017 the Organ Procurement and Transplantation Network established medical eligibility for those who are candidates for simultaneous liver kidney transplantation (SLK) that included a "safety net" allocation priority for individuals who undergo liver transplantation alone and develop new or ongoing progressive renal impairment.

Individuals are eligible for an SLK if they have a sustained acute kidney injury (≥ 6 weeks of requiring \geq once-weekly dialysis or a GFR of

≤25 mL/min tested weekly) or chronic kidney disease (GFR ≤60 mL/min for >90 days and a subsequent worsening of renal function of GFR ≤30 mL/min or need for regular dialysis). The hope in those not meeting these criteria is that their renal function may recover, minimizing the transplantation of kidneys into individuals who may not need them.

To qualify for the safety net, individuals must be listed for kidney transplantation within 1 year of their transplantation with either a GFR less than 20 mL/min or a need for dialysis. If individuals are listed through this safety net protocol, they are prioritized on the kidney transplantation wait list.

REFERENCE

Wilk AR, Booker SE, Stewart DE, et al. Developing simultaneous liver-kidney transplant medical eligibility criteria while providing a safety net: A 2-year review of the OPTN's allocation policy. *Am J Transplant*. 2021;21(11):3593-3607. doi:10.1111/ajt.16761

Question 15

A 48-year-old man with primary sclerosing cholangitis develops worsening liver tests is found to have a 2.1-cm hilar mass on imaging. This diagnosis is confirmed to be cholangiocarcinoma after undergoing a percutaneous biopsy of the lesion. There is no evidence of intrahepatic or extrahepatic metastases on any imaging. An endoscopic ultrasound of regional lymph nodes with lymph node aspiration does not show any evidence of malignancy.

Which of the following is most accurate regarding transplantation in this patient?

- A. Transplantation for hilar cholangiocarcinoma should not be considered as it has a poor prognosis and universal risk of recurrence
- B. Transplantation should be pursued as soon as possible with the lack of metastatic disease or lymph node involvement
- C. Transplantation should be pursued in this patient if he is able to undergo neoadjuvant chemotherapy and radiation and a repeat negative staging workup prior to transplantation
- D. Transplantation can be considered for hilar cholangiocarcinoma, but the history of percutaneous biopsy would be a contraindication

CORRECT ANSWER: D

RATIONALE

Historically, hilar cholangiocarcinoma was considered a contraindication for liver transplantation because of the nearly universal recurrence and subsequent mortality. Transplantation is now considered an option in many centers in those with early-stage unresectable hilar cholangiocarcinoma after data published from the Mayo Clinic showed acceptable outcomes in a highly selected cohort of patients. In their study, patients were only considered for transplantation if their tumor was smaller than 3 cm, they had no evidence of metastases, and they had never undergone percutaneous biopsy due to the risk of peritoneal seeding. In those who were candidates, patients received neoadjuvant therapy that included both radiation and systemic chemotherapy, followed by repeat staging before transplantation.

Transplantation centers have since developed individualized protocols for transplantation for early-stage hilar cholangiocarcinoma. In addition to a requirement for neoadjuvant therapy and repeat staging after treatment, the Organ Procurement and Transplantation Network mandates that transperitoneal biopsy (either by endoscopic ultrasound or percutaneous approaches) be an exclusion criterion in any institutional protocol.

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Sudan D, DeRoover A, Chinnakotla S, et al. Radio-chemotherapy and transplantation allow long-term survival for nonresectable hilar cholangiocarcinoma. *Am J Transplant.* 2002;2(8):774-779. doi:10.1034/j.1600-6143.2002.20812.x

Question 16

A 52-year-old man with compensated cirrhosis of the liver undergoes an upper endoscopy and colonoscopy for evaluation of iron deficiency anemia. His colonoscopy is normal and upper endoscopy reveals a mosaic mucosal pattern with a “snake-skin” appearance.

Which of the following would be most appropriate for the management of this patient’s anemia?

- A. Endoscopic management with argon-plasma coagulation
- B. Initiation of a nonselective beta-blocker and iron supplementation
- C. Initiation of a twice-daily proton pump inhibitor and iron supplementation
- D. Placement of a transjugular intrahepatic portosystemic shunt

CORRECT ANSWER: B

RATIONALE

This patient has evidence of portal hypertensive gastropathy (PHG). First-line therapy consists of iron supplementation for anemia and nonselective beta-blockers. Transjugular intrahepatic portosystemic shunt can be considered if first-line measures fail, although its overall efficacy is not clear. PHG is a result of portal hypertension, and acid suppression is unlikely to be beneficial. Argon-plasma coagulation has not been shown to be beneficial for PHG.

REFERENCES

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Diges-*

tive Diseases Self-Education Program 10. American Gastroenterological Association; 2022.

Ripoll C, Garcia-Tsao G. Treatment of gastropathy and gastric antral vascular ectasia in patients with portal hypertension. *Curr Treat Options Gastroenterol.* 2007;10(6):483-494. doi:10.1007/s11938-007-0048-5

Question 17

A 72-year-old man with decompensated cirrhosis with ascites presents for follow-up. His primary concern is that he has been losing muscle mass in his face and extremities leading to a change in his overall appearance. He describes his typical diet as skipping breakfast and eating an early lunch and then a large dinner around 6 pm each day. He feels that his diet is overall very healthy and that he gets in the recommended amounts of protein and calories that have previously been recommended to him. He has remained active, regularly walking 2 miles daily and doing strength exercises with light weights 3 times weekly.

Which of the following recommendations should be made first for the management of his sarcopenia?

- A. Limit aerobic exercise and weightlifting
- B. Increase food intake to meet recommended calorie and protein goals
- C. Alter the timing of his meals, as this is likely worsening his sarcopenia independent of calorie and protein intake
- D. Initiate a workup for other causes of weight loss as sarcopenia is not explained by his liver disease

CORRECT ANSWER: C

RATIONALE

Loss of muscle mass (otherwise known as sarcopenia) is a frequent complication of cirrhosis that has been associated with a variety of adverse clinical outcomes. In this setting, specific recommendations should be given regarding total caloric (30-35 kg/kg daily) and protein (1.2-1.5 g/kg

daily) intake for any individual with cirrhosis. An important consideration is that the liver's glycogen reserves are depleted in cirrhosis and even short periods of fasting can lead to muscle breakdown. This was shown in a randomized controlled trial comparing a late-evening nutritional supplement (of 710 kcal) with a similar supplement given during the day. Despite similar total energy and protein intakes in the 2 groups in this study, those who had a late-evening snack were found to have an additional 2 kilograms (4.4 pounds) of lean tissue over the course of 12 months.

This patient is fasting for prolonged periods of time (roughly 16 hours a day between meals), which will lead to worsening of his sarcopenia. Physical activity should be encouraged, and sarcopenia is frequently seen with liver disease.

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Question 18

A 57-year-old woman is hospitalized with an acute variceal hemorrhage and undergoes endoscopic variceal ligation (EVL, or “banding”). She presents for follow-up 1 week later. Since discharge, she has been doing well, without any evidence of recurrent bleeding. Her laboratory test results are notable for a hemoglobin of 9.1 g/dL (reference range, 12-16 g/dL), thrombocytopenia, and a normal bilirubin, liver enzymes, and creatinine.

Which of the following strategies would be most appropriate to prevent recurrent variceal hemorrhage?

- A. Perform a transjugular intrahepatic portosystemic shunt (TIPS)
- B. Repeat endoscopy with EVL every 3 months until eradication then plan intermittent endoscopies for monitoring
- C. Repeat endoscopy with EVL every 4 weeks until eradication, then plan intermittent endoscopies for monitoring
- D. Start a nonselective beta-blocker (NSBB) and repeat endoscopy only if recurrent of bleeding
- E. Start a NSBB and repeat endoscopy with EVL every 4 weeks until eradication, then intermittent endoscopies for monitoring

CORRECT ANSWER: E

RATIONALE

Individuals who survive an episode of acute variceal hemorrhage have a bleeding risk of around 60% if untreated. Current recommendations are for a combination of EVL and NSBB to prevent rebleeding in this population. The answers that do not incorporate combination therapy are incorrect as combination therapy has been shown to be superior to EVL alone at preventing rebleeding. TIPS is incorrect and recommended as a rescue therapy in those who experience recurrent bleeding despite management with EVL and NSBB combination therapy.

REFERENCES

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology*. 2017;65(1):310-335. doi:10.1002/hep.28906

Question 19

A 49-year-old man with compensated cirrhosis of the liver undergoes an upper endoscopy and colonoscopy for evaluation of iron deficiency anemia. His colonoscopy is normal and upper endoscopy reveals multiple red spots and linear areas of erythema converging on the pylorus.

In addition to endoscopic therapy, which of the following have been shown to reduce bleeding from this lesion?

- A. Initiation of a nonselective beta-blocker
- B. Liver transplantation
- C. Initiation of a proton pump inhibitor
- D. Placement of a transjugular intrahepatic portosystemic shunt

CORRECT ANSWER: B

RATIONALE

This patient has evidence of gastric antral vascular ectasia (GAVE; commonly known as “watermelon stomach”). First-line therapy consists of endoscopic electrocoagulation or laser therapy and multiple sessions are often needed. For refractory cases, surgical antrectomy can be performed, albeit with significant morbidity. A variety of case reports and case series have shown that GAVE can resolve after liver transplantation. No medication has been clearly shown to be beneficial for the treatment of GAVE.

Unlike portal hypertensive gastropathy and varices, bleeding from GAVE does not respond to measures that reduce portal pressure. Proton pump inhibitors would not be effective as this is unrelated to excess production of acid.

REFERENCES

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Ripoll C, Garcia-Tsao G. Treatment of gastropathy and gastric antral vascular ectasia in patients with

portal hypertension. *Curr Treat Options Gastroenterol*. 2007;10(6):483-494. doi:10.1007/s11938-007-0048-5

Question 20

A 65-year-old man with cirrhosis secondary to hepatitis C virus infection presents to his primary care provider to discuss his poor sleep quality and excessive sleepiness during the day. Prior attempts to optimize management of his hepatic encephalopathy and change the timing of his diuretics to avoid nighttime awakenings have been unsuccessful.

Which of the following is most accurate regarding pharmacologic treatment options in this patient?

- A. Zolpidem does not undergo hepatic clearance and can be used long term
- B. Hydroxyzine worsens sleep measures compared with placebo
- C. Melatonin improves sleep quality when given in short duration
- D. Pharmacotherapy for sleep disturbances has not been studied in individuals with cirrhosis; all sleep agents should be avoided

CORRECT ANSWER: C

RATIONALE

Sleep disturbances are relatively common in individuals with cirrhosis. When present, clinicians should consider inadequately treated hepatic encephalopathy (which can lead to sleep-wake reversal) as well as sleep hygiene, which includes ensuring lactulose and diuretics are timed to avoid nocturnal awakenings. Medications that have been studied in small randomized controlled trials for sleep disturbances in cirrhosis include melatonin, zolpidem, and hydroxyzine. Each of these studies showed improvement in sleep quality when given over a short period of time (with the studies ranging from 10 days to 4 weeks in duration). There are no studies looking at use of these medications for longer duration. Zolpidem has been studied in

this population, but in general should be avoided due to hepatic clearance and not for long terms. Hydroxyzine was studied in a small trial and showed improvement in sleep measures compared with placebo.

REFERENCES

De Silva AP, Niriella MA, Ediriweera DS, et al. Low-dose melatonin for sleep disturbances in early-stage cirrhosis: A randomized, placebo-controlled, cross-over trial. *JGH Open*. 2020;4(4):749-756. Published 2020 May 18. doi:10.1002/jgh3.12356

Sharma MK, Kainth S, Kumar S, et al. Effects of zolpidem on sleep parameters in patients with cirrhosis and sleep disturbances: A randomized, placebo-controlled trial. *Clin Mol Hepatol*. 2019;25(2):199-209. doi:10.3350/cmh.2018.0084

Spahr L, Coeytaux A, Giostra E, Hadengue A, Annoni JM. Histamine H1 blocker hydroxyzine improves sleep in patients with cirrhosis and minimal hepatic encephalopathy: a randomized controlled pilot trial. *Am J Gastroenterol*. 2007;102(4):744-753. doi:10.1111/j.1572-0241.2006.01028.x

Question 21

A 62-year-old woman with decompensated cirrhosis undergoes an upper endoscopy in the setting of hematemesis. She is found to have a gastric varix that extends from the gastroesophageal junction along the lesser curvature of the stomach with active hemorrhage, as well as esophageal varices without any evidence of recent bleeding.

Which of the following therapies would be most appropriate?

- A. Attempt to obliterate the varix using tissue adhesives (ie, butyl-cyanoacrylate)
- B. Manage the patient medically and consult surgery for splenectomy

- C. Perform balloon tamponade using the gastric balloon of the Sengstaken-Blakemore tube
- D. Perform an endoscopic variceal ligation (EVL) at the area of active bleeding

CORRECT ANSWER: D

RATIONALE

This patient has type 1 gastric varices (GOV1), which are located along the lesser curvature of the stomach. Bleeding from GOV1 should be managed similarly to bleeding from esophageal varices. This patient does not need adhesive (glue) therapy as this patient is a candidate for standard endoscopic therapies. Balloon tamponade can control bleeding temporarily but should be viewed as a 'bridge' to more definitive therapies. If this individual had gastric varices in the fundus (type 2 or type 3 gastric varices, also referred to as GOV2 and isolated gastric varices type 3 [IGV3], respectively), standard endoscopic therapies would be unlikely to control bleeding and other treatments, such as endoscopic "glue", transjugular intrahepatic portosystemic shunt with embolization of fundal varices could be considered. Splenectomy can be considered in the presence of splenic vein thrombosis.

REFERENCE

Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology*. 2017;65(1):310-335. doi:10.1002/hep.28906

Question 22

A 55-year-old man with alcohol-related liver disease presents for transplantation evaluation. He was hospitalized for jaundice and ascites 8 months before and quit drinking alcohol at that time.

Since then, his jaundice and ascites have progressively resolved. He has small varices that have not bled and has never had encephalopathy.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.8	3.5-5.5
Bilirubin (total), serum, mg/dL	1.3	0.3-1.0
Creatinine, serum, mg/dL	0.8	0.7-1.5
International normalized ratio	1.4	<1.1
Sodium, serum, mEq/L	140	136-145

His current laboratory test results shown above.

Based on these results, his calculated Model for End-Stage Liver Disease (MELD)-Na score is 10. He recently was found to have a 1.2-cm liver mass on multiphase computed tomography imaging without arterial phase enhancement or washout and no prior cross-sectional imaging to compare.

Which of the following is most accurate regarding this patient’s indications for liver transplantation?

- A. He currently does not have any clear indications for liver transplantation and can be considered if his liver tests or liver lesion change over time
- B. He should undergo transplantation evaluation as his primary indication for liver transplantation is the presence of cirrhosis
- C. He should undergo transplantation evaluation as his primary indication for liver transplantation is a MELD score
- D. He should undergo transplantation evaluation as his primary indication for liver transplantation is an advanced Child-Pugh score
- E. He should undergo transplantation evaluation as his primary indication for liver transplantation is hepatocellular carcinoma

CORRECT ANSWER: A

RATIONALE

With alcohol abstinence, this patient has had an improvement in his liver function and has transitioned from decompensated to compensated cirrhosis. His laboratory test results are consistent with a relatively low MELD-Na score (10) and Child-Pugh class A cirrhosis. He will need to con-

tinue to be followed and undergo serial imaging but, at this time, he does not have clear indications for transplantation.

The risks of liver transplantation do not clearly outweigh the benefits in this individual. Although transplantation is clearly beneficial in individuals with advanced liver disease with high MELD scores, a survival advantage with transplantation is only seen after MELD scores are greater than 17.

He also lacks significant decompensations that are associated with worse survival, as evidenced by his Child-Pugh score. His liver lesion is not clearly a hepatocellular carcinoma, given its small size and lack of characteristic features on imaging.

REFERENCE

Martin P, DiMartini A, Feng S, Brown R Jr, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Hepatology*. 2014;59(3):1144-1165. doi:10.1002/hep.26972

Merion RM, Schaubel DE, Dykstra DM, Freeman RB, Port FK, Wolfe RA. The survival benefit of liver transplantation. *Am J Transplant*. 2005;5(2):307-313. doi:10.1111/j.1600-6143.2004.00703.x

Question 23

A 66-year-old man with decompensated cirrhosis secondary nonalcoholic fatty liver disease is diagnosed with hepatocellular carcinoma after undergoing imaging for abdominal pain. His prior liver decompensations include ascites and hepatic encephalopathy, both controlled on medications. His other comorbidities include diabetes and mild

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	2.6	3.5–5.5
Bilirubin (total), serum, mg/dL	4.2	0.3–1.0
Creatinine, serum, mg/dL	1.3	0.7–1.5
International normalized ratio	2.1	<1.1
Sodium, serum, mEq/L	136	136–145

chronic kidney disease. His functional status is limited, and he notes that he spends around two-thirds of the day in bed or a chair.

His blood tests are shown above.

Based on these results, his MELD-Na (Model for End-Stage Liver Disease) score is 24 and his Child-Pugh class is C.

Multiphasic computed tomography (CT) imaging of his liver and noncontrast CT imaging of his lungs shows 5 hepatocellular carcinomas in his liver, the largest of which is 4.3 cm with evidence of invasion of the portal vein. His imaging does not show any evidence of metastatic disease.

Which of the following is the most appropriate next step in the treatment of his HCC?

- A. Referral for liver transplantation
- B. System chemotherapy and transarterial chemoembolization
- C. Systemic chemotherapy
- D. Supportive care only

CORRECT ANSWER: D

RATIONALE

This patient has end-stage hepatocellular carcinoma (Barcelona Clinic Liver Cancer stage D) given his poor functional status and poor liver function (Child-Pugh class C). This corresponds to a poor survival (<3 months) and treatment should be supportive. He is not a transplantation candidate based off tumor burden and vascular invasion (outside of “Milan criteria”). His advanced liver disease makes him a poor candidate for systemic and locoregional therapies.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 24

A 58-year-old woman with decompensated nonalcoholic fatty liver disease (NASH) cirrhosis and hepatocellular carcinoma (HCC) presents for transplantation evaluation. She has a history of coronary artery disease requiring percutaneous coronary intervention with stenting 2 years before, diabetes being treated with insulin (with a recent hemoglobin A_{1c} of 7.6%), and morbid obesity (based off her body mass index of 36 kg/m² with comorbid conditions). As part of her transplantation evaluation, she undergoes a left and right heart catheterization in the setting of an abnormalities on echocardiogram (ejection fraction, 60%–65%; right ventricular systolic pressure, >45 mmHg), and stress testing (largely normal except for a likely attenuation artifact near the diaphragm). Her left heart catheterization reveals prior stenting and nonobstructive coronary artery disease. Her right heart catheterization shows a mean pulmonary arterial pressure greater than 50 mmHg with an elevated pulmonary vascular resistance and normal pulmonary wedge pressure. She undergoes imaging that reveals a 4.2-cm HCC without vascular invasion or metastatic spread. Which of the following represents her biggest barrier/contraindication to transplantation?

- A. History of HCC
- B. Body mass index greater than 35 kg/m²
- C. History of pulmonary hypertension
- D. History of coronary artery disease and diabetes

CORRECT ANSWER: C

RATIONALE

This patient underwent a right heart catheterization after her echocardiogram revealed evidence of pulmonary hypertension (with right ventricular systolic pressure [RVSP] > 45 mmHg). Her right heart catheterization is consistent with severe pulmonary hypertension (mean pulmonary artery pressure [MPAP] > 45 mmHg), which should be considered a contraindication to transplantation if this cannot be improved. A Mayo Clinic case series showed a 100% mortality in those who received a transplant with an MPAP greater than 50 mmHg, and current guidelines only recommend pursuing transplantation if these patients achieve an adequate response to medical therapy. Her HCC is still within transplantation criteria for HCC (Milan criteria). Body mass index greater than 40 kg/m² is a relative contraindication to transplantation (but not an absolute contraindication). Her diabetes is under good control and her coronary artery disease has been adequately revascularized. Given her HCC, liver transplantation would likely provide her the best chance at long-term survival.

REFERENCE

Martin P, DiMartini A, Feng S, Brown R Jr, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Hepatology*. 2014;59(3):1144-1165. doi:10.1002/hep.26972

Question 25

A 62-year-old man with alcohol-related cirrhosis presents for evaluation. He has been abstinent

from alcohol for over 1 year and his only decompensation is ascites controlled with low-dose diuretics. He has never experienced variceal hemorrhage. His blood tests are shown below.

Based on these results, his MELD (Model for End-Stage Liver Disease) score is 13 and Child-Pugh grade is B. He undergoes an upper endoscopy that reveals multiple columns of varices in his lower esophagus that do not flatten with insufflation with multiple red patches of discoloration overlying them.

Which of the following would be the most appropriate management for this patient?

- A. Obtain an echocardiogram and refer patient for placement of a transjugular intrahepatic portosystemic shunt
- B. Perform endoscopic variceal ligation and start propranolol 20 mg twice daily and titrating to a resting heart rate of 55-60 bpm
- C. Discuss risks of variceal bleeding and plan repeat endoscopies at yearly intervals
- D. Start carvedilol 6.25 mg nightly and increase to twice-daily dosing in 3 days

CORRECT ANSWER: D

RATIONALE

This patient is at significant risk of variceal hemorrhage. The most important predictor of variceal hemorrhage is the size of the varices, with individuals with large varices experiencing their first hemorrhage at a rate of 15% per year. Other predictors of bleeding are also present in this patient, including the presence of red wale signs on endoscopy and Child-Pugh class B or C cirrhosis. In this setting, interventions should be pursued

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.3	3.5-5.5
Bilirubin (total), serum, mg/dL	2.1	0.3-1.0
Creatinine, serum, mg/dL	1.0	0.7-1.5
International normalized ratio	1.4	<1.1
Platelet count, plt/ μ L	83,000	150,000-450,000

to prevent variceal hemorrhage from occurring, a strategy known as primary prophylaxis. Three different nonselective beta-blockers (nadolol, propranolol, and carvedilol) can be recommended for primary prophylaxis in individuals with cirrhosis and medium/large varices that have not bled. Although the dose of propranolol and nadolol need to be adjusted to the maximally tolerated dose or a heart rate goal, carvedilol can be uptitrated to a dose of 12.5 mg daily. An alternate strategy that can be considered is endoscopic variceal ligation, which has been shown in randomized controlled trials to be as effective as nonselective beta-blockers for primary prophylaxis. The combination of NSBB and variceal ligation has been associated with more side effects without reduction in variceal hemorrhage risk in this population that has not had active bleeding. TIPS placement is not recommended for the primary prophylaxis based off trials of prophylactic surgical shunts showing a higher rate of encephalopathy and a trend toward higher mortality.

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Question 26

A 47-year-old woman with compensated cirrhosis presents to your office for routine follow-up. She reports feeling at her baseline except for new

shortness of breath over the past 2 months. She does not report chest pain, lightheadedness, or lower extremity swelling. Her blood pressure is 109/70 mmHg, heart rate is 72 bpm, oxygen saturation, 95% on room air, and she is afebrile. On examination, she has decreased breath sounds on the right base and new mild abdominal distention. You arrange for an abdominal ultrasound, which shows trace ascites. Chest radiography shows a new right-sided pleural effusion and no other abnormalities. Her laboratory test results are notable for the following shown below.

Which of the following is the next best step in the management of this patient?

- A. Arrange for chest computed tomography
- B. Arrange for chest tube placement
- C. Start furosemide 40 mg orally daily
- D. Start oral fluid restriction
- E. Start spironolactone 50 mg orally daily

CORRECT ANSWER: E

RATIONALE

Hepatic hydrothorax is present in 5% to 10% of patients with ascites. The management of hepatic hydrothorax is similar to the management of ascites. Starting spironolactone 50–100 mg orally daily is the initial approach to treat ascites (and thus, hepatic hydrothorax). The patient has cirrhosis and given the possibility of hepatic hydrothorax in this setting and confirmed on radiography, chest computed tomography is not necessary. Furosemide 40 mg orally daily is incorrect given the recommended diuretic to start in patients with ascites is monotherapy with spironolactone. Chest tube placement should never be performed in the setting of hepatic hydrothorax, even in diuretic refractory cases. Because her serum sodium is normal, fluid restriction is not indicated.

Laboratory Test	Result	Reference Range
Creatinine, serum, mg/dL	0.8	0.7-1.5
Potassium, serum, mEq/L	3.8	3.5-5.0
Sodium, serum, mEq/L	136	136-145

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 27

A 73-year-old man is admitted to the hospital for progressive abdominal distention. He reports decreased appetite and decreased oral intake, yet a weight gain of 15 pounds over the past month due to his new distention. He has known hypertension, atrial fibrillation, hypercholesterolemia, fatty liver, and type 2 diabetes mellitus. His examination is notable for abdominal distention with shifting dullness and 2+ pitting edema bilaterally on his legs.

His laboratory test results on admission are shown below.

A paracentesis is performed with the following lab results: total polymorphonuclear count, 100/ μ L; total ascites protein, 2.7 g/dL; and albumin, 1.8 g/dL.

What is the most likely source of his ascites?

- A. Abdominal tuberculosis
- B. Cardiac failure
- C. Nonalcoholic steatohepatitis
- D. Peritoneal carcinomatosis
- E. Portal vein thrombosis

CORRECT ANSWER: B

RATIONALE

The patient has evidence of portal hypertension given the serum-ascites albumin gradient (SAAG) greater than 1.1. The ascites protein level shows a high total protein (>2.5 g/dL) indicating normal sinusoids as is seen in cardiac ascites that have not yet “capillarized.” Hepatic causes of portal hypertension will have a low total protein in the ascites fluid (<2.5 g/dL). Abdominal tuberculosis, portal vein thrombosis, and peritoneal carcinomatosis do not have associated portal hypertension as suggested by his SAAG.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 28

A 64-year-old man currently listed for liver transplantation for hepatocellular carcinoma (HCC). He has ascites due to decompensated cirrhosis, and his HCC has been ablated. The patient is hospitalized with new renal failure. His creatinine is 3.2 mg/dL today, up from admission yesterday’s value of 2.4 mg/dL and up from a baseline of 1.0 mg/dL last week. He has grade 2 encephalopathy. The team has discontinued his outpatient spironolactone and furosemide and started intravenous albumin

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.0	3.5-5.5
Alkaline phosphatase, serum, U/L	170	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	54	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	36	10-40
Bilirubin (total), serum, mg/dL	2.1	0.3-1.0
Blood urea nitrogen (BUN), serum or plasma, mg/dL	25	8-20
Creatinine, serum, mg/dL	1.3	0.7-1.5
International normalized ratio	1.3	<1.1
Potassium, serum, mEq/L	3.6	3.5-5.0
Sodium, serum, mEq/L	130	136-145

for volume expansion. On examination, he has abdominal distention and asterixis. He had a recent computed tomography to evaluate for HCC that was done 3 days prior to admission. Computed tomography showed area of prior ablation with increase in size of this lesion and enhancement of the portal vein concerning for thrombus. His last bowel movement was formed but appeared to be melena. His hemoglobin is 7.9 g/dL and esophagogastroduodenoscopy (EGD) 4 months ago showed small varices with no high-risk stigmata.

What is the best next step in the management of this patient?

- A. Hold lactulose given the history of melena
- B. Referral for liver transplantation given the history of hepatorenal syndrome
- C. Repeat EGD given the history of varices
- D. Resume low-dose diuretics given the history of distention
- E. Transfuse 2 units of red blood cells given the history of anemia

CORRECT ANSWER: C

RATIONALE

Patients with cirrhosis should have repeat EGD with any signs of clinical decompensation. The use of lactulose for encephalopathy should not be impacted by the presence of melena. Given the patient's renal injury, diuretics should be held. Conservative transfusion strategy should be implemented in the setting of cirrhosis so that portal hypertension is not worsened. The patient does not have HRS as that is a diagnosis of exclusion and he has other reasons for acute kidney injury (intravenous contrast agent, volume depletion). In addition, there is concern for tumor thrombus on his recent computer tomography so transplantation would not be an option.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 29

A 42-year-old man with alcohol-related cirrhosis has been admitted multiple times for hepatic encephalopathy. He is routinely discharged home with prescriptions for lactulose and rifaximin. He has improvement of his symptoms while hospitalized.

What could be a potential cause of his recurrent encephalopathy and frequent admissions?

- A. Lactulose use for 4-5 liquid bowel movements (BMs) daily
- B. Methadone use at a stable dose daily
- C. Plant-based normal protein diet daily
- D. Rifaximin dosed twice daily
- E. Sodium intake of 2000 mg daily

CORRECT ANSWER: A

RATIONALE

Patients with encephalopathy should have 2-3 soft (not liquid) BMs daily. This patient may be developing dehydration from frequent BMs, and this could be precipitating his encephalopathy. His methadone dose is stable and likely not contributing to his symptoms of confusion. A plant-based normal protein diet can be tried to help with encephalopathy so this would not worsen it. Rifaximin twice daily is appropriate dosing for encephalopathy. Sodium intake of 2000 mg daily is recommended in cirrhosis and should not precipitate encephalopathy episodes.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 30

A 52-year-old man with longstanding, active alcohol use disorder and no routine healthcare presents to the emergency department with variceal bleeding. He was resuscitated appropriately, and esophagogastroduodenoscopy performed within

12 hours of admission showed large bleeding varices (GOV2), which were banded.

Which imaging finding below is the best explanation for his current presentation?

- A. Acute necrotizing pancreatitis
- B. Multifocal hepatocellular carcinoma and portal vein thrombosis
- C. Pancreatic pseudocyst compression of the stomach
- D. Pancreatitis with splenic artery aneurysm
- E. Splenomegaly with splenic vein thrombosis

CORRECT ANSWER: B

RATIONALE

This patient has GOV2 suggesting portal hypertension that is from an intrahepatic source. Multifocal hepatocellular carcinoma could cause portal vein thrombosis and subsequent variceal bleeding especially if he has not had routine hepatology care to evaluate for hepatocellular carcinoma. Splenic artery aneurysm would not lead to bleeding esophageal varices. Pseudocyst compression of the stomach would not predispose to formation of varices. Splenic vein thrombosis would cause prehepatic portal hypertension and isolated gastric varices in addition to splenomegaly. The presence of necrotizing pancreatitis does not lead to esophageal variceal bleeding.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 31

A 57-year-old woman with mild chronic obstructive pulmonary disease (COPD) and hepatitis C virus (HCV)-related cirrhosis and ascites presents to your office after 4.8 cm lesion was noted on

ultrasound done for hepatocellular carcinoma (HCC) surveillance. A subsequent magnetic resonance imaging measured the lesion at 5.5 cm with evidence of arterial enhancement and washout on delayed images. Her liver enzymes including bilirubin are normal. She would like to know her options for treatment.

What treatment option is appropriate to discuss with her at this time?

- A. Locoregional therapy with transarterial radioembolization
- B. Hospice referral given her decompensated cirrhosis and HCC
- C. Noninvasive systemic therapy based on her COPD history
- D. Surgical resection for definitive management
- E. Transjugular biopsy of the lesion followed by locoregional therapy

CORRECT ANSWER: A

RATIONALE

This patient has HCC diagnosed by imaging, which is appropriate when the features of HCC are present in someone with cirrhosis. Liver biopsy would not be necessary in this case, which makes transjugular biopsy of the lesion followed by locoregional therapy incorrect. The patient would not be a candidate for liver transplantation based on her tumor size at this time but could be considered if her tumor is downsized appropriately after transarterial radioembolization. Hospice is not appropriate given there are treatment options for her. Surgery is not recommended given her ascites/portal hypertension. She would be a candidate for systemic therapy if locoregional therapy was not an option, but her laboratory tests results are normal so locoregional therapy should be considered first.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 32

A 54-year-old man presents to your office for a new diagnosis of cirrhosis. The patient has a history of hepatitis C virus (HCV) and has never been treated. In addition to discussing HCV therapy, you review other ways to improve his overall liver health. The risk of hepatocellular carcinoma (HCC) was discussed and the benefits of screening were reviewed.

Which intervention listed should be used to screen for HCC in this patient?

- A. Ultrasound with alpha fetoprotein (AFP) every year indefinitely
- B. Ultrasound with AFP every 6 months until HCV is eradicated, then yearly
- C. Ultrasound with AFP every 6 months indefinitely
- D. Ultrasound with AFP every 6 months until no longer a transplant candidate
- E. Ultrasound with AFP every 6 months until decompensation, then every 3 months

CORRECT ANSWER: C

RATIONALE

Patients with cirrhosis have an increased risk of HCC. Screening patients routinely allows for earlier detection and provides the greatest number of treatment options. Studies demonstrate that a combination of serum alpha fetoprotein levels along with ultrasound every 6 months provides earlier detection of HCC and reduces mortality. Screening with yearly ultrasounds is incorrect due to the possibility of rapid tumor growth rate, limiting successful therapies. Once someone has cirrhosis, they should continue with HCC screening indefinitely; currently, there are no modifications to this recommendation in the setting of sustained virologic response. There are benefits to early detection of HCC (ie, offering locoregional therapy) regardless of whether the patient is no longer a transplant candidate, so screening should continue. There is no recommendation to alter HCC screening intervals in the setting of decompensated cirrhosis.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 33

A 69-year-old woman was given a liver transplant for hepatitis B virus (HBV)-related cirrhosis and hepatocellular carcinoma (HCC) with a detectable HBV DNA of 4500 IU/mL and positive HBV surface antigen at the time of transplantation. She accepted a partial liver from her son and is doing well after her living donor transplantation. In addition to her routine immunosuppression, she was given instructions on her HBV management after transplantation.

Which of the following medication(s) should be added to her discharge medication list?

- A. Intravenous (IV) HBV immunoglobulin
- B. IV immunoglobulin (IVIG)
- C. IV HBV immunoglobulin and entecavir daily
- D. IVIG and entecavir daily
- E. IVIG, IV HBV immunoglobulin, and entecavir daily

CORRECT ANSWER: C

RATIONALE

HBV recurs after transplantation, and the risk is modified by oral nucleos(t)-ide analogues (NAs) used daily. Given the risk of HBV reactivation is highest in the early days after transplantation when immunosuppression is greatest, it is recommended to also treat patients with IV HBV immunoglobulin in addition to a NA such as entecavir. This is especially true when patients have detectable HBV DNA at the time of transplantation and are at increased risk of HCC (her past history of HCC would place her at increased risk). There is no role for IVIG in treatment of HBV after transplantation.

Laboratory Test	Result Last Week	Result Today	Reference Range
Alkaline phosphatase, serum, U/L	109	118	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	36	87	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	34	79	10-40
Bilirubin (total), serum, mg/dL	0.9	1.0	0.3-1.0
Creatinine, serum, mg/dL	1.1	--	0.7-1.5
International normalized ratio	1.0	1.0	<1.1

REFERENCE
Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 34

A 66-year-old man with chronic hepatitis C virus (HCV; genotype 1a) undergoes successful liver transplantation at Model for End-stage Liver Disease (MELD) of 21 before his HCV treatment. Six weeks after his surgery, he is seen in outpatient clinic. His immunosuppression treatment consists of tacrolimus, prednisone, and mycophenolate mofetil. He also takes trimethoprim-sulfamethoxazole and ganciclovir for prophylaxis. He does not report fevers, only mild incisional numbness and discomfort in the upper abdomen. His laboratory test results from last week and today are shown above.

What is the best next step in his disease management after transplantation?

- A. Check right upper quadrant ultrasound for a biliary stricture or leak
- B. Counsel him on avoiding any alcohol or supplements postoperatively
- C. Perform a liver biopsy to rule out acute rejection versus recurrent HCV
- D. Stop the trimethoprim-sulfamethoxazole due to concerns for drug-induced liver injury
- E. Start ledipasvir/sofosbuvir to treat his HCV

CORRECT ANSWER: C

RATIONALE
HCV recurs after transplantation in the new graft 100% of the time. Rates of graft failure were higher before the discovery of direct-acting antiviral agents. In this case, performing a liver biopsy to rule out acute rejection versus recurrent HCV is correct. The diagnosis of recurrent HCV vs acute cellular rejection can be challenging. Liver biopsy allows for diagnostic accuracy, and the effective treatment plan to be executed. Stopping the trimethoprim-sulfamethoxazole due to concerns for drug-induced liver injury is incorrect as there should be an attempt to rule out more serious causes of liver injury and the prophylaxis is generally well tolerated. Checking right upper quadrant ultrasound for a biliary stricture or leak is incorrect due to normal cholestatic laboratory tests. Starting ledipasvir/sofosbuvir to treat his HCV is incorrect because there should be documentation of recurrent HCV as the cause of liver test abnormality before starting ledipasvir/sofosbuvir.

Counseling him on avoiding any alcohol or supplements postoperatively pertains to all patients post-transplantation, but his risk factors for recurrent HCV or rejection warrant more diagnostic testing.

REFERENCE
Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 35

A 55-year-old woman with nonalcoholic steatohepatitis (NASH) cirrhosis is admitted to the

hospital for melena. On initial examination, she is noted to have a few beats of asterixis. She has no prior history of hepatic encephalopathy (HE). She had an esophagogastroduodenoscopy with banding of esophageal varices and no further melena.

On admission, her ammonia level was 108 $\mu\text{mol/L}$ (reference range, 15–45 $\mu\text{mol/L}$). She was started on oral lactulose 15 mL twice daily with 1 soft bowel movement (BM) daily and prompt resolution of her asterixis.

What medication regimen is appropriate for her HE upon discharge?

- A. Lactulose 15 mL twice daily for a goal of 2–3 soft BMs daily
- B. Lactulose 15 mL daily for a goal of 2–3 soft BMs daily
- C. No medication for her HE is needed
- D. Rifaximin 550 mg twice daily and lactulose 15 mL twice daily for a goal of 2–3 soft BMs daily
- E. Rifaximin 550 mg twice daily and lactulose 15 mL 3 times daily for a goal of 2–3 soft BMs daily

CORRECT ANSWER: C

RATIONALE

Precipitants for HE are present in 80% of cases including gastrointestinal bleeding. No medication for her HE encephalopathy is correct given that her asterixis on initial examination was mild and likely precipitated by her variceal bleed. She had prompt resolution of her asterixis when admitted after her bleeding resolved. The ammonia level should not be used to guide therapy in HE. The remaining choices are incorrect due to her not requiring any medication at discharge.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 36

A 49-year-old man presents to your office for follow-up of hepatic encephalopathy (HE). He has alcohol-related cirrhosis and has been sober for over 10 years. His treatment for HE is rifaximin 550 mg twice daily and lactulose 30 mL three times daily, and he is having 3 soft bowel movements (BM) daily. He has continued sleep-wake cycle alterations, and he is more forgetful. He reports that with more frequent lactulose, his BMs have become very loose, which causes incontinence.

What is the best next step in the management of his HE?

- A. Arrange for electroencephalogram
- B. Arrange for psychometric and neuropsychological testing
- C. Change dietary protein intake from plant sources to animal sources
- D. Check ammonia levels; if elevated, add an additional dose of lactulose
- E. Order imaging to evaluate for splanchnic vessel shunts

CORRECT ANSWER: E

RATIONALE

Occasionally, there are cases of recurrent HE that are unresponsive to standard therapy. Ordering imaging to evaluate for splanchnic vessel shunts is correct since investigating for shunts can be a treatable cause of HE. If present, the shunts could be embolized to help with HE. Checking ammonia levels and, if elevated, adding an additional dose of lactulose is incorrect as ammonia does not correlate with HE. An electroencephalogram and psychometric and neuropsychological testing are helpful in research and diagnosis, but his presentation is classic for covert HE so no further diagnostic information is needed. Changing dietary protein intake from plant sources to animal sources is incorrect as changing to plant sources may be helpful rather than changing to animal sources of protein.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 37

A 56-year-old woman with hepatitis C virus-related cirrhosis presents to your office for follow-up. She has a history of refractory ascites, and transjugular intrahepatic portosystemic shunt (TIPS) was performed 5 months ago. After TIPS, she developed hepatic encephalopathy (HE) and was started on lactulose 30 mL three times daily and has 3 to 4 soft bowel movements daily. She reported continued difficulty with lethargy and somnolence. Rifaximin 550 mg twice daily was started 1 month ago. Today, she is here with her wife and no improvement in her symptoms is reported.

What are the best next steps in management of her HE?

- A. Perform abdominal ultrasound for hepatocellular carcinoma screening
- B. Perform echocardiogram for evaluation of right heart failure
- C. Refer to interventional radiology for TIPS embolization
- D. Refer to neurology for possible ongoing seizures
- E. Refer to nutrition for discussion regarding a high protein diet

CORRECT ANSWER: C

RATIONALE

TIPS can precipitate HE and in cases where stan-

dard medical treatments do not control symptoms, there may be a need to embolize or reduce the size of the shunt. Perform echocardiogram for evaluation of right heart failure is incorrect as there are no signs of heart failure. She should not be placed on a high protein diet because that will worsen her HE. She is not likely to have ongoing seizures since her symptoms followed TIPS. She had her TIPS 5 months ago and thus does not need hepatocellular carcinoma screening at this time.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 38

A 21-year-old man presents to the emergency department with jaundice and confusion. He was accompanied by his roommate who returned from a weekend away and found the patient wandering about the house. The patient is an avid weightlifter and often takes supplements to enhance his performance and has no prior history of liver disease.

Laboratory test results are shown below.

Which type of encephalopathy does this presentation illustrate?

- A. Type A
- B. Type B
- C. Type C – episodic hepatic encephalopathy, precipitated
- D. Type C – persistent HE, severe
- E. Type C – persistent HE, treatment-dependent

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	910	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	408	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	379	10-40
Bilirubin (total), serum, mg/dL	17	0.3-1.0
International normalized ratio	3.5	<1.1

CORRECT ANSWER: A**RATIONALE**

Hepatic encephalopathy has been associated with different states of liver injury and thus, has differing clinical course, severity, and fatality, which are important to recognize. Type A is associated with acute liver failure, and this is the correct answer based on this patient's history and presentation. Type B is associated with bypass shunts in the absence of cirrhosis. Type C is gradual onset, rarely fatal, and associated with cirrhosis and portosystemic shunting. There are subcategories of type C (persistent or episodic) outlined in the reference by Ferenci et al, which further classify the forms of HE related to cirrhosis.

REFERENCES

Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei AT. Hepatic encephalopathy—definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th World Congresses of Gastroenterology, Vienna, 1998. *Hepatology*. 2002;35(3):716-721. doi:10.1053/jhep.2002.31250

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 39

A 63-year-old man with nonalcoholic steatohepatitis (NASH) cirrhosis presents to the hospital with new worsening abdominal distention. He has no signs of encephalopathy. Ultrasound with doppler

shows no evidence of thrombosis or tumor, but large volume ascites. A diagnostic paracentesis of 1L was performed for fluid analysis and shows total polymorphonuclear count, 78 cells/ μ L; total ascites protein, 0.9 g/dL; and ascites albumin, 1.2 g/dL.

His other laboratory test results shown below.

Which therapy is the best next step in the management of his ascites?

- A. Ciprofloxacin daily
- B. Intravenous (IV) albumin
- C. IV albumin, midodrine, and octreotide
- D. IV ceftriaxone
- E. Spironolactone daily

CORRECT ANSWER: E**RATIONALE**

Spironolactone daily is correct as spironolactone daily is an appropriate diuretic to start in a patient with ascites. It should be titrated every 3 to 5 days and furosemide can be started in addition to spironolactone. IV ceftriaxone is incorrect because the patient does not have spontaneous bacterial peritonitis. IV albumin is incorrect because the volume of fluid removed in the paracentesis does not warrant albumin infusion. Ciprofloxacin daily is incorrect because though the patient has a low ascites protein, the patient does not meet other criteria to warrant spontaneous bacterial peritonitis prophylaxis with ciprofloxacin. This can be used in hospitalized patients with liver failure and renal failure where transplantation is imminent. IV albumin, midodrine, and octreotide is incorrect because the patient does not have hepatorenal syndrome.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	2.9	3.5-5.5
Bilirubin (total), serum, mg/dL	1.9	0.3-1.0
Creatinine, serum, mg/dL	1.1	0.7-1.5
International normalized ratio	1.2	<1.1
Potassium, serum, mEq/L	3.9	3.5-5.0
Sodium, serum, mEq/L	132	136-145

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.1	3.5–5.5
Bilirubin (total), serum, mg/dL	1.4	0.3–1.0
Creatinine, serum, mg/dL	1.2	0.7–1.5
Hemoglobin, plasma, mg/dL	7	<5.0
International normalized ratio	1.2	<1.1
Leukocyte count, cells/ μ L	8000	4000–11,000
Potassium, serum, mEq/L	3.9	3.5–5.0
Sodium, serum, mEq/L	136	136–145

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 40

A 49-year-old woman with cirrhosis presents to the emergency department with her family for lethargy and confusion. Your interview is conducted in the emergency department while she awaits a hospital bed. Initial vital signs include blood pressure, 100/60 mmHg; heart rate, 65 bpm; oxygen saturation, 98% on room air. She is afebrile, somnolent, and anicteric with normal cardiopulmonary examination, and she has abdominal distention on examination, with no tenderness. She has asterixis.

Her laboratory test results are shown above.

Which intervention is the best next step in her management and should be done before transfer out of the emergency department?

- A. Discussion about the need for liver transplantation
- B. Perform abdominal ultrasound for hepatocellular carcinoma screening
- C. Perform diagnostic paracentesis
- D. Perform esophagogastroduodenoscopy for variceal screening
- E. Perform head computed tomography

CORRECT ANSWER: C

RATIONALE

It is vital to perform a diagnostic paracentesis in patients who present with decompensation. Spontaneous bacterial peritonitis can precipitate acute-on-chronic liver failure and so early diagnosis is critical. Patients may present with fever or abdominal pain but about one-third present with only encephalopathy so diagnostic paracentesis is correct. The remaining answers are reasonable to consider depending on her clinical course over the hospitalization; however, it would not have the same urgency as diagnostic paracentesis.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 41

A 64-year-old woman with primary biliary cholangitis-related cirrhosis and liver transplant 2 years ago is presenting for follow-up in your office. She is taking tacrolimus 2 mg twice daily for immunosuppression, levothyroxine 75 mcg daily for her hypothyroidism, and calcium with vitamin D. She does not report any herbal medicines or other medications.

Her laboratory test results last week are shown at the top of the following page.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.8	3.5–5.5
Alkaline phosphatase, serum, U/L	160	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	31	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	30	10–40
Bilirubin (total), serum, mg/dL	1.0	0.3–1.0
Creatinine, serum, mg/dL	0.7	0.7–1.5
International normalized ratio	0.8	<1.1

Tacrolimus level is unchanged from previous values at 5.0 ng/mL (reference range, 5.0–15.0 ng/mL). She has no symptoms of pruritus, confusion, jaundice, or melena. Her weight has been stable (body mass index of 24 kg/m²), and she does not report abdominal distention. She drinks 1 glass of wine 2 times a year.

What would be the most likely finding on liver biopsy to explain her liver test abnormalities?

- A. Florid bile duct lesion
- B. Endotheliitis
- C. Bile duct plugging
- D. Steatohepatitis
- E. Bridging fibrosis with nodules

CORRECT ANSWER: A

RATIONALE

Recurrent primary biliary cholangitis (PBC) can occur after transplantation. Given the laboratory values, there is a likelihood that her rise in alkaline phosphatase represents this process, and the biopsy would show a florid bile duct lesion, which is a classic finding in patients with PBC making Answer A the correct choice. Answer B would be correct in acute cellular rejection (ACR); however, she had a transplantation 2 years ago and her lab pattern is more cholestatic, which would

be inconsistent with ACR. Also, her tacrolimus level is close to normal range and stable. Bile duct plugging would be seen in patients with jaundice or drug-induced liver injury with higher bilirubin. Steatohepatitis would be seen in patients with fatty liver from nonalcoholic fatty liver disease (NAFLD) or alcohol, which is not supported by her body mass index or alcohol history. Finally, the patient has no clinical signs of cirrhosis by examination or laboratory tests against the idea of bridging fibrosis.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 42

A 32-year-old woman presents with fulminant hepatic failure in the setting of autoimmune hepatitis (AIH). She was placed status 1A in the region for transplantation and received a liver within 48 hours of listing.

Her laboratory results immediately after transplantation and 6 hours later are shown below. She remains intubated and somnolent despite light sedation.

Laboratory Test	Result After Transplantation	Result 6 hours Later	Reference Range
Bilirubin (total), serum, mg/dL	21	35	0.3–1.0
Creatinine, serum, mg/dL	2.5	3.6	0.7–1.5
International normalized ratio	2.2	4.5	<1.1

Laboratory Test	Result After Surgery	Result 8 hours After Surgery	Result 12 hours After Surgery	Reference Range
Albumin, serum, g/dL	3.8	--	--	3.5-5.5
Alkaline phosphatase, serum, U/L	204	220	320	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	276	389	490	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	300	345	485	10-40
Bilirubin (total), serum, mg/dL	3.0	3.4	4.6	0.3-1.0

What is the cause of her persistent liver failure?

- A. Acute cellular rejection
- B. Cytomegalovirus hepatitis
- C. Hepatic artery thrombosis
- D. Primary graft nonfunction
- E. Severe autoimmune hepatitis

CORRECT ANSWER: D

RATIONALE

Primary graft nonfunction is a serious and rare complication that occurs after transplantation. The patient’s clinical worsening within 24 hours suggests this diagnosis. She has a history of autoimmune hepatitis (AIH); however, in the setting of high-dose steroids, it would be unusual to have her numbers continue to rise as it would in severe AIH. Cytomegalovirus hepatitis would not present so acutely in the setting of ganciclovir. Hepatic artery thrombosis is more common and could also be considered; however, primary graft nonfunction is more consistent with her laboratory test results and clinical deterioration. Acute cellular rejection would not present with such laboratory test abnormalities in the setting of high-dose prednisone or this soon after transplantation.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 43

A 45-year-old woman with alcohol-related cirrhosis

received a living donor transplant from her sister. Her surgery was without immediate complication.

She remains intubated in the intensive care unit and laboratory test results are trended after the surgery. They are shown above.

What is the best next step in treatment of these abnormal liver enzymes?

- A. Abdominal ultrasound to assess biliary anastomosis stricture
- B. Doppler ultrasound to assess hepatic artery
- C. Liver biopsy to rule out cytomegalovirus hepatitis
- D. Nuclear medicine study to assess for biliary leak
- E. Pulse steroids to treat acute cellular rejection

CORRECT ANSWER: B

RATIONALE

Hepatic artery thrombosis is a complication that can present acutely and early after transplantation and requires detection with doppler ultrasound when suspected. There are some patients who require surgical repair when this is discovered. Liver biopsy may be appropriate but assessing for hepatic artery thrombosis should be done first. The possibility of acute cellular rejection is possible; however, a biopsy would be indicated before starting pulse steroids. A biliary leak is possible after an operation, but her laboratory test results would likely be more cholestatic in nature. Biliary strictures do not occur after transplantation so acutely so abdominal ultrasound to assess biliary anastomosis stricture is incorrect.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	150	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	55	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	69	10-40
Bilirubin (total), serum, mg/dL	2.0	0.3-1.0

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 44

A 57-year-old man is following up with you after liver transplantation was completed 3 weeks prior for hepatitis B virus/hepatocellular carcinoma. He reports feeling fatigued, with low energy and vague abdominal pain. On examination, vitals show temperature of 38.2 °C, heart rate of 101 bpm, blood pressure of 120/78 mmHg, and oxygen saturation of 98% on room air. You immediately arrange for admission to the hospital. Laboratory test results done on arrival are shown on the above.

Blood cultures are pending, chest radiography shows mild bibasilar atelectasis. His medications include prednisone, entecavir, tacrolimus, mycophenolate mofetil, trimethoprim-sulfamethoxazole, and ganciclovir.

What is the most likely cause of his current presentation?

- A. Bacterial infection from enterococcus
- B. Bacterial infection from pneumocystis
- C. Fungal infection from aspergillosis
- D. Viral infection from cytomegalovirus
- E. Viral infection from Epstein-Barr virus

CORRECT ANSWER: A

RATIONALE

Bacterial infection from enterococcus is correct because most commonly, bacterial infections

present within 1 month of transplantation. He is reporting abdominal pain and has a fever so a biliary source is most likely. Although pneumonia is a possible bacterial infection, bacterial infection from pneumocystis would be unusual given he had a normal oxygen saturation, and his chest radiography does not show any consolidation. Viral infection from cytomegalovirus would be unusual given his prophylaxis and the laboratory test results do not support Epstein-Barr virus hepatitis.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 45

A 43-year-old woman with history of liver transplantation for hepatitis B virus/hepatocellular carcinoma cirrhosis presents to your office for follow-up. Her transplantation was 3 months ago, and she has been feeling well. She is adherent to her medications. Her transaminase levels were elevated for the past few weeks at 2 to 3 times the upper limit of normal, and you arranged for an outpatient liver biopsy last week. She is here to review the pathology.

Which biopsy findings listed below would support your decision to bolus with high-dose steroids?

- A. Central endotheilitis
- B. Councilman bodies
- C. Ground glass hepatocytes
- D. Hepatic foam cell arteriopathy
- E. Noncaseating biliary granulomas

CORRECT ANSWER: A

RATIONALE

Central endotheliitis is correct because it represents 1 of the 3 major histologic features associated with acute cellular rejection, which requires boluses of high-dose steroids. The other 2 features are a mixed inflammatory infiltrate in the portal triad (primary lymphocytic) and destructive or nondestructive nonsuppurative cholangitis involving interlobular bile duct epithelium. Ground glass hepatocytes is incorrect as that describe features seen in hepatitis B virus. Noncaseating biliary granulomas is incorrect as that describes findings seen in primary biliary cholangitis. Councilman bodies is noted in viral-related liver injury. hepatic foam cell arteriopathy is seen in chronic rejection, which is not treated with boluses of high-dose steroids.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 46

A 72-year-old woman is admitted from a nursing home for confusion. She has a history of liver transplantation for hepatitis B virus 10 years ago and was placed in assisted living by her family over 5 years ago due to progressive dementia. Her immunosuppression regimen is listed as tacrolimus 1 mg twice daily. She has noted liver test abnormalities on admission are shown below.

On examination, she has mild asterixis, normal cardiopulmonary examination with no abdominal tenderness.

What is the best next step in her management?

- A. Check ammonia level
- B. Check tacrolimus level
- C. Perform liver biopsy
- D. Start high-dose steroids
- E. Start N-acetylcysteine

CORRECT ANSWER: B

Rationale Checking the tacrolimus level is correct. Tacrolimus levels may be low and if so, that could be a cause of her elevated liver tests. Alternatively, if elevated, that could be a cause of confusion and renal insufficiency. Starting high-dose steroids would be correct if a liver biopsy shows signs of rejection or autoimmune injury but this would not be done before checking her tacrolimus level.

Checking ammonia would not be helpful in the management of her confusion and should not be used to guide therapy. She does not have clinical or laboratory signs of acute liver failure at this time, so N-acetylcysteine is not indicated.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.3	3.5–5.5
Alkaline phosphatase, serum, U/L	198	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	220	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	187	10–40
Bilirubin (total), serum, mg/dL	2.0	0.3–1.0
Creatinine, serum, mg/dL	2.2	0.7–1.5
International normalized ratio	2.2	<1.1
Potassium, serum, mEq/L	4.9	3.5–5.0
Sodium, serum, mEq/L	139	136–145

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.8	3.5–5.5
Alkaline phosphatase, serum, U/L	112	30–120
Aminotransferase, serum alanine (ALT, SGPT), U/L	37	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	38	10–40
Bilirubin (total), serum, mg/dL	1.0	0.3–1.0
Blood urea nitrogen (BUN), serum or plasma, mg/dL	32	8–20
Creatinine, serum, mg/dL	2.4	0.7–1.5
Glucose, plasma (fasting), mg/dL	112	70–99
Hemoglobin A _{1c} , %	6.0	4.0–5.6
International normalized ratio	1.2	<1.1
Potassium, serum, mEq/L	3.9	3.5–5.0
Sodium, serum, mEq/L	138	136–145
Tacrolimus, blood (trough), ng/mL	10	5.0–15.0

Question 47

A 52-year-old man with history of liver transplantation 5 years ago for alcohol-related cirrhosis comes to see you in follow-up. He has a history of hypertension, hyperlipidemia, and recent diagnosis of type 2 diabetes. His body mass index is 31 kg/m². He takes tacrolimus 4 mg twice daily for immunosuppression. Other medications are amlodipine 5 mg daily, metformin 500 mg twice daily, and multivitamin. Laboratory test results that were completed before the office visit are shown above.

What would be your approach to his elevated creatinine?

- A. Decrease amlodipine to 2.5 mg daily
- B. Decrease tacrolimus to 3 mg twice daily
- C. Stop amlodipine and switch to furosemide
- D. Stop metformin and switch to insulin
- E. Stop tacrolimus and switch to cyclosporine

CORRECT ANSWER: B

RATIONALE

Decreasing tacrolimus to 3 mg twice daily is correct as the first step to possible calcineurin inhibitors renal toxicity is to lower the dose of tacroli-

mus while following the transaminase levels. His current tacrolimus level is on the higher range of normal and lower levels should be targeted if transaminase levels remain normal. He has metformin for his diabetes which should be safe for his renal function while not worsening his obesity risk (as insulin does). His amlodipine is likely not contributing to renal injury and furosemide would not be indicated as a substitute for amlodipine in this setting. Cyclosporine would potentially worsen his hypertension and could still contribute to renal injury so should not be tried.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 48

A 58-year-old woman is seeing you in clinic for follow-up after a liver transplantation done 10 years ago for autoimmune hepatitis (AIH). Other history is notable for fatty liver on ultrasound, class 1 obesity (body mass index, 32 kg/m²), hypercholesterolemia, hypertension, and osteopenia. She has a long history of low-dose prednisone used to control her AIH and has gained weight steadily since transplantation. She is taking tacrolimus 2 mg twice daily.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.5	3.5-5.5
Alkaline phosphatase, serum, U/L	110	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	42	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	48	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0
Creatinine, serum, mg/dL	1.4	0.7-1.5
Tacrolimus, blood (trough), ng/mL	5.9	5.0-15.0

Routine laboratory test results are shown above. Her labs have been in this range for several years. What therapeutic intervention would be best to manage her liver care moving forward?

- A. Check ultrasound with alpha fetoprotein every 6 months
- B. Perform a liver biopsy
- C. Perform elastography now and yearly
- D. Refer to bariatric surgery
- E. Stop prednisone

CORRECT ANSWER: B

RATIONALE

Performing a liver biopsy is correct; a liver biopsy is indicated at this time. She has mildly abnormal laboratory test results, which have persisted for some time. Her underlying AIH, worsening obesity, and status as a liver transplant recipient would make it important to assess her inflammation and level of fibrosis. Performing elastography now and yearly is reasonable to assess fibrosis; however, it does not help to evaluate the cause of her abnormal liver enzymes. She is not at risk for hepatocellular carcinoma so checking ultrasound with alpha fetoprotein every 6 months is incorrect. She does not meet criteria for bariatric surgery with a body mass index lower than 35 kg/m²). Prednisone should not be discontinued without understanding her underlying pathology.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 49

A 78-year-old man with liver transplantation performed 20 years ago for alcohol-related cirrhosis is seeing you in clinic for routine follow-up. He is adherent to his immunosuppressive medications (tacrolimus 1 mg twice daily and mycophenolate mofetil 500 mg twice daily) and has normal laboratory test results. He has no new medical diagnoses since the last visit. He drinks only 1 cocktail once a month and has done so for several years. He had a screening colonoscopy last year with diverticulosis. He has become more active year-round now that he spends winters in Florida. He has lost 10 pounds over the past year with walking 4 miles daily and making changes to his diet.

From what complication would he be at high risk to develop after transplantation?

- A. Chronic (ductopenic) rejection
- B. Colon cancer
- C. Non-melanomatous skin cancer
- D. Recurrent alcohol-related cirrhosis
- E. Type 2 diabetes mellitus

CORRECT ANSWER: C

RATIONALE

Nonmelanomatous skin cancer is correct. Given his immunosuppression and sun exposure by living and exercising in Florida, he is at increased risk for skin cancer. He would be at low risk for chronic rejection given his normal laboratory test results and maintenance on immunosuppression. He has lost 10 pounds, which should lower his risk of diabetes. He is up to date with colonoscopy so

has a low risk of colon cancer. He drinks minimal alcohol so would likely not develop recurrent cirrhosis, though given his history of cirrhosis from alcohol, that is something to follow with laboratory tests and clinical findings.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Question 50

A 44-year-old man with primary sclerosing cholangitis (PSC)-related cirrhosis presents for follow-up after receiving a living donor transplant 4 years ago. He has been adherent to immunosuppression with tacrolimus 4 mg twice daily. His body mass index is the normal range, and he has borderline hypertension. His laboratory test results are listed below.

What routine screening examination would be important to implement given his clinical history?

- A. Colonoscopy yearly for colon cancer detection
- B. Dual-energy X-ray absorptiometry scans yearly for osteopenia detection
- C. Hemoglobin A1C yearly for type 2 diabetes detection
- D. Ultrasound yearly for hepatocellular carcinoma detection
- E. Urinalysis yearly for proteinuria and tacrolimus-related injury detection

CORRECT ANSWER: A

RATIONALE

Colonoscopy yearly for colon cancer detection is correct based on the increased risk of colon cancer in patients with PSC who have received a liver transplant. This is also true of patients with ulcerative colitis. There is no indication to screen yearly for osteopenia. The patient is not at risk for hepatocellular carcinoma (HCC) so would not need ultrasound and yearly screening for HCC is inaccurate. Calcineurin inhibitors toxicity is not detected with proteinuria, and yearly urinalysis is not recommended. Hemoglobin A1c yearly is not routinely recommended in patients after liver transplantation and should be done based on clinical picture.

REFERENCE

Garcia-Tsao G. Cirrhosis and liver transplantation. In: Teitelman M, Marino D, Shah N, eds. *Digestive Diseases Self-Education Program 10*. American Gastroenterological Association; 2022.

Laboratory Test	Result	Reference Range
Albumin, serum, g/dL	3.9	3.5-5.5
Alkaline phosphatase, serum, U/L	98	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	30	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	28	10-40
Bilirubin (total), serum, mg/dL	0.7	0.3-1.0
Creatinine, serum, mg/dL	0.7	0.7-1.5
Tacrolimus, blood (trough), ng/mL	6.3	5.0-15.0

CHAPTER 8

Gastrointestinal and liver disease in pregnancy

Rich Bloomfeld, MD and Claire Meyer, MD

Question 1

A 32-year-old woman who is 26 weeks pregnant presents with bloody diarrhea. She has never experienced this before. She reports that for about 3 weeks she has about 4 loose bowel movements daily with urgency and some blood with each bowel movement. She has no new medications and no recent travel.

After sending stool tests to evaluate for infection, what would be the next best step in evaluation?

- A. Barium enema
- B. Abdominal ultrasound
- C. Sigmoidoscopy
- D. Upper endoscopy
- E. Defer evaluation until after delivery

CORRECT ANSWER: C

RATIONALE

Endoscopy can be performed in pregnant patients, and sigmoidoscopy is low risk during pregnancy. A diagnostic sigmoidoscopy should be performed in pregnant women with a clear indication. An upper endoscopy or imaging with barium enema or ultrasound is unlikely to yield a diagnosis in a patient with bloody diarrhea.

REFERENCES

De Lima A, Galjart B, Wisse PHA, Bramer WM, van der Woude CJ. Does lower gastrointestinal

endoscopy during pregnancy pose a risk for mother and child? - a systematic review. *BMC Gastroenterol.* 2015;15(1). doi:10.1186/s12876-015-0244-z

Friedel D. Gastrointestinal endoscopy in the pregnant woman. *World J Gastrointest Endosc.* 2014;6(5). doi:10.4253/wjge.v6.i5.156

Question 2

A 22-year-old woman who is 18 weeks pregnant presents to the hospital with abdominal pain and abnormal liver tests. An abdominal ultrasound reveals cholelithiasis and choledocholithiasis with a 5-mm stone present in the distal common bile duct.

What is the best therapeutic option?

- A. Cholecystectomy with common duct exploration
- B. Placement of a percutaneous biliary drain
- C. Endoscopic ultrasound with drainage of the biliary tree
- D. Endoscopic retrograde cholangiopancreatography with stone extraction
- E. Defer therapy until after delivery

CORRECT ANSWER: D

RATIONALE

Endoscopic retrograde cholangiopancreatography is considered the best intervention in pregnant patients who have known bile duct pathology that requires intervention. It should be performed by an experienced endoscopist and efforts should be made to minimize radiation exposure. With the presence of abnormal liver function tests and pain, to prevent the progression to cholangitis, the common bile duct stone should be removed. The percutaneous drain would not be an option to consider in this case, endoscopic ultrasound would not remove the offending problem, and delaying until after delivery would be dangerous as it could progress. Surgery could likely be avoided with endoscopic retrograde cholangiopancreatography.

REFERENCES

Friedel D. Gastrointestinal endoscopy in the pregnant woman. *World J Gastrointest Endosc.* 2014;6(5). doi:10.4253/wjge.v6.i5.156

Shergill AK, Ben-Menachem T, Chandrasekhara V, et al. Guidelines for endoscopy in pregnant and lactating women. *Gastrointest Endosc.* 2012;76(1). doi:10.1016/j.gie.2012.02.029

Question 3

A 34-year-old healthy woman who is had a baby 2 months earlier presents with odynophagia. Symptoms have persisted for a week, and you elect to evaluate with an upper endoscopy with propofol for sedation. She informs you that she is breastfeeding her infant.

What is the best course of action?

- A. Counsel her to stop breastfeeding before endoscopy
- B. Change the sedation plan to meperidine and midazolam
- C. Counsel her to pump and discard breast milk for at least 24 hours after endoscopy
- D. Counsel her to resume breastfeeding after endoscopy

- E. Change the evaluation to a barium esophagram

CORRECT ANSWER: D

RATIONALE

Endoscopy is compatible with breastfeeding and the levels of propofol seen in breast milk after anesthesia are low enough that interruption of breastfeeding is likely not warranted. Meperidine should be avoided during breastfeeding.

REFERENCES

Nitsun M, Szokol JW, Saleh HJ, et al. Pharmacokinetics of midazolam, propofol, and fentanyl transfer to human breast milk. *Clin Pharmacol Ther.* 2006;79(6). doi:10.1016/j.clpt.2006.02.010

Shergill AK, Ben-Menachem T, Chandrasekhara V, et al. Guidelines for endoscopy in pregnant and lactating women. *Gastrointest Endosc.* 2012;76(1). doi:10.1016/j.gie.2012.02.029

Question 4

A 29-year-old woman is in her second trimester of pregnancy and reports heartburn. She has no dysphagia or odynophagia. She has had insufficient improvement with nonpharmacologic treatments.

What is the best first-line pharmacologic therapy?

- A. Sodium bicarbonate
- B. Aluminum-magnesium hydroxide
- C. Famotidine
- D. Omeprazole
- E. Metoclopramide

CORRECT ANSWER: B

RATIONALE

Heartburn is very common during pregnancy and if lifestyle modifications are not successful then pharmacologic therapy should be used. Antacids containing aluminum or magnesium hydroxide are generally low risk and used as first-

line therapy. Sodium bicarbonate should not be used in pregnancy. Famotidine, omeprazole, and metoclopramide can be used to treat heartburn in pregnancy if antacids are unsuccessful but are not first-line agents to be used.

REFERENCE

Body C, Christie JA. Gastrointestinal Diseases in Pregnancy. Nausea, Vomiting, Hyperemesis Gravidarum, Gastroesophageal Reflux Disease, Constipation, and Diarrhea. *Gastroenterol Clin North Am.* 2016;45(2). doi:10.1016/j.gtc.2016.02.005

Question 5

A 20-year-old woman is 6 weeks pregnant and is experiencing mild nausea without vomiting throughout the day, and she seeks your advice.

What is the best initial strategy?

- A. Nonpharmacologic options
- B. Doxylamine/vitamin B6
- C. Metoclopramide
- D. Ondansetron
- E. Steroids

CORRECT ANSWER: A

RATIONALE

Nausea is the most common gastrointestinal complaint in pregnancy and can often be managed with nonpharmacologic treatments such as small, frequent, low-fat meals. Triggers should be avoided and hydration encouraged. Pharmacologic treatments including doxylamine/vitamin B6, metoclopramide, ondansetron, and steroid should be used judiciously.

REFERENCE

McParlin C, O'Donnell A, Robson SC, et al. Treatments for hyperemesis gravidarum and nausea and vomiting in pregnancy: A systematic review. *JAMA - J Am Med Assoc.* 2016;316(13). doi:10.1001/jama.2016.14337

Question 6

A 28-year-old woman with a history of Crohn's ileitis presents to her gastroenterologist for pre-pregnancy counseling. She was diagnosed with Crohn's ileitis at age 18 and has never had surgery. She has been treated with 3 courses of prednisone and is currently in clinical remission on adalimumab. Her C-reactive protein is 0.6 mg/dL, and her fecal calprotectin is normal. She has heard that people with Crohn's disease are less likely to have children, and she is concerned about infertility.

What is the best information to counsel this patient?

- A. She has a decrease in fecundity due to having Crohn's ileitis
- B. She has a decrease in fecundity due to her history of steroid use
- C. She has a decrease in fecundity due to her history of adalimumab use
- D. She has normal fecundity with quiescent disease

CORRECT ANSWER: D

RATIONALE

Rates of infertility in people with Crohn's disease in remission are similar to the general population. Although prior surgeries may affect fertility rates, a history of steroid or adalimumab use do not.

REFERENCE

Bonthala N, Kane S. Updates on Women's Health Issues in Patients with Inflammatory Bowel Disease. *Curr Treat Options Gastroenterol.* 2018;16(1). doi:10.1007/s11938-018-0172-4

Question 7

A 34-year-old woman with a history of ulcerative colitis presents to her gastroenterologist for pre-pregnancy counseling. She was diagnosed with extensive ulcerative colitis at age 27 and did not respond to mesalamine. She was then in clinical

remission for years on infliximab. She recently lost response to infliximab despite dose optimization. She is currently having about 6 bowel movements daily with some urgency and bleeding.

She is recently married and would like to become pregnant soon.

What is the best advice regarding management of ulcerative colitis in this patient?

- A. She should proceed with pregnancy as this may induce remission
- B. She should use aminosalicylates to induce remission before pregnancy
- C. She should use vedolizumab to induce remission before pregnancy
- D. She should use azathioprine to induce remission before pregnancy
- E. She should undergo proctocolectomy with ileal pouch-anal anastomosis before pregnancy

CORRECT ANSWER: C

RATIONALE

Active inflammatory bowel disease at the onset of pregnancy increases the risk for adverse pregnancy outcomes, so ulcerative colitis should be treated to induce remission before a planned pregnancy. In this patient who has lost response to infliximab, treatment with an alternate biologic such as vedolizumab is the best option. She has already failed an aminosalicylate in the past and azathioprine is not effective at inducing remission.

Proctocolectomy with ileal pouch-anal anastomosis will increase the risk of infertility in this patient who desires pregnancy.

REFERENCE

McConnell RA, Mahadevan U. Pregnancy and the Patient with Inflammatory Bowel Disease: Fertility, Treatment, Delivery, and Complications. *Gastroenterol Clin North Am.* 2016;45(2). doi:10.1016/j.gtc.2016.02.006

Question 8

A 33-year-old man with ulcerative colitis presents to his gastroenterologist for a routine clinic visit. He was diagnosed with severe ulcerative colitis 4 years ago and is currently on sulfasalazine, azathioprine, and infliximab for maintenance of remission. He mentions that he and his wife have been trying to conceive for 6 months but have been unsuccessful.

What would be the best advice for this patient regarding male fertility in patients with ulcerative colitis?

- A. Severe ulcerative colitis is associated with male infertility
- B. Sulfasalazine is associated with male infertility
- C. Azathioprine is associated with male infertility
- D. Infliximab is associated with male infertility
- E. Ulcerative colitis and these medications are not associated with male infertility

CORRECT ANSWER: B

RATIONALE

Sulfasalazine is associated with male infertility due to reversible sperm dysfunction and changing sulfasalazine to mesalamine should be considered. Ulcerative colitis, along with azathioprine and infliximab use, are not known to affect male fertility.

REFERENCE

Shin T, Okada H. Infertility in men with inflammatory bowel disease. *World J Gastrointest Pharmacol Ther.* 2016;7(3). doi:10.4292/wjgpt.v7.i3.361

Question 9

A 27-year-old woman with Crohn's disease presents to her gastroenterologist for an urgent clinic visit. She was diagnosed with Crohn's ileitis with perianal disease 5 years ago; she was treated with infliximab and azathioprine and achieved clinical remission. She would like to become pregnant, so she discontinued both azathioprine and infliximab

4 months ago. She developed mild abdominal pain and diarrhea with about 4 bowel movements daily 2 weeks ago and her primary care physician prescribed budesonide.

What is the best advice regarding potential pregnancy complications in this patient?

- A. Budesonide is associated with increased pregnancy complications
- B. Azathioprine is associated with increased pregnancy complications
- C. Infliximab is associated with increased pregnancy complications
- D. Active Crohn's disease is associated with increased pregnancy complications
- E. She does not have increased risk for pregnancy complications

CORRECT ANSWER: D

RATIONALE

Women with active Crohn's disease at the time of conception are at increased risk for adverse pregnancy outcomes. Budesonide is not associated with pregnancy complications. Infliximab can be used throughout pregnancy without a clear increase in risk. Although there has been concern about thiopurine use during pregnancy, it may be used if needed, and is not clearly associated with adverse pregnancy outcomes.

REFERENCE

McConnell RA, Mahadevan U. Pregnancy and the Patient with Inflammatory Bowel Disease: Fertility, Treatment, Delivery, and Complications. *Gastroenterol Clin North Am.* 2016;45(2). doi:10.1016/j.gtc.2016.02.006

Question 10

A 30-year-old woman with Crohn's disease presents to her gastroenterologist for pre-pregnancy counseling. She was diagnosed with Crohn's colitis 5 years ago and was steroid dependent. She was initiated on azathioprine and has remained in

clinical remission for about 2 years. She would like to become pregnant in the next year and is concerned about the effects of azathioprine on pregnancy and breastfeeding.

What is the best management strategy for this patient?

- A. Discontinue azathioprine 3 months before pregnancy
- B. Discontinue azathioprine 3 months before delivery
- C. Continue azathioprine through pregnancy, but advise not to breast-feed
- D. Continue azathioprine through pregnancy and breastfeeding

CORRECT ANSWER: D

RATIONALE

Active Crohn's disease is associated with adverse pregnancy outcomes, so maintaining remission is important to a healthy pregnancy. Although there has historically been concern about the use of thiopurines, such as azathioprine and mercaptopurine, during pregnancy and breastfeeding, they are not clearly associated with adverse pregnancy outcomes and may be continued through pregnancy and breastfeeding to maintain remission.

REFERENCE

Kanis SL, de Lima-Karagiannis A, de Boer NKH, van der Woude CJ. Use of Thiopurines During Conception and Pregnancy Is Not Associated With Adverse Pregnancy Outcomes or Health of Infants at One Year in a Prospective Study. *Clin Gastroenterol Hepatol.* 2017;15(8). doi:10.1016/j.cgh.2017.02.041

Question 11

A 30-year-old woman with a history of ulcerative colitis presents to her gastroenterologist for a routine appointment. She was diagnosed with ulcerative colitis 4 years ago and has been in clinical remission on vedolizumab for the past 2

years. She is currently 30 weeks pregnant and is planning to breastfeed. She is due for an infusion in 4 weeks.

What is the best management strategy for this patient?

- A. Hold vedolizumab until after delivery
- B. Hold vedolizumab until after she has completed breastfeeding
- C. Infuse vedolizumab and discourage breastfeeding
- D. Infuse vedolizumab and encourage breastfeeding

CORRECT ANSWER: D

RATIONALE

Biologic drugs for inflammatory bowel disease, including vedolizumab, can be used throughout pregnancy to maintain remission and it is not necessary to hold the drug during the third trimester. Breast milk has been found to have low drug levels and breastfeeding can be encouraged in most women with inflammatory bowel disease, including those on biologic drugs.

REFERENCE

Matro R, Martin CF, Wolf D, Shah SA, Mahadevan U. Exposure Concentrations of Infants Breast-fed by Women Receiving Biologic Therapies for Inflammatory Bowel Diseases and Effects of Breastfeeding on Infections and Development. *Gastroenterology*. 2018;155(3). doi:10.1053/j.gastro.2018.05.040

Question 12

A 29-year-old woman is referred to a gastroenterologist by her obstetrician-gynecologist. She has had problems with infertility and is undergoing evaluation. During this evaluation, she was found to have an elevated tissue transglutaminase IgA level. An upper endoscopy is scheduled to confirm the diagnosis of celiac disease.

What is the best advice for this patient regarding infertility?

- A. Untreated celiac disease is associated with infertility
- B. HLA-DQ8 is associated with infertility
- C. An elevated tissue transglutaminase IgA level is associated with infertility
- D. A gluten-free diet is associated with infertility

CORRECT ANSWER: A

RATIONALE

Reproductive concerns, including infertility and miscarriage, may occur in some people with undiagnosed celiac disease. Some physicians may test for celiac disease as part of a workup for infertility or recurrent pregnancy loss. Impaired fertility has been associated with undiagnosed celiac disease, but has not been associated with HLA-DQ8, tissue transglutaminase IgA level, or a gluten-free diet.

REFERENCE

Zugna D, Richiardi L, Akre O, Stephansson O, Ludvigsson JF. A nationwide population-based study to determine whether coeliac disease is associated with infertility. *Gut*. 2010;59(11). doi:10.1136/gut.2010.219030

Question 13

A 31-year-old woman presents to discuss management of Crohn's disease. She has had right lower quadrant abdominal pain and diarrhea with 6 bowel movements daily for about 6 weeks. An abdominopelvic computed tomography suggested thickening of the terminal ileum, and a colonoscopy last week revealed ulceration in the terminal ileum and cecum. Biopsies revealed chronic active ileitis without granulomas. She is recently married and desires pregnancy when she is feeling well.

Which of the following medications would be contraindicated for this patient's Crohn's disease?

- A. Azathioprine
- B. Ustekinumab
- C. Sulfasalazine
- D. Budesonide
- E. Methotrexate

CORRECT ANSWER: E

RATIONALE

Methotrexate is a known teratogen and should be discontinued 3 to 6 months before conception. Other inflammatory bowel disease medications—including sulfasalazine, budesonide, azathioprine, and ustekinumab—are not contraindicated in women planning pregnancy.

REFERENCE

Herfarth HH, Kappelman MD, Long MD, Isaacs KL. Use of Methotrexate in the Treatment of Inflammatory Bowel Diseases. *Inflamm Bowel Dis*. 2016;22(1). doi:10.1097/MIB.0000000000000589

Question 14

A 35-year-old man with ulcerative colitis presents to his gastroenterologist for a routine clinic visit. He was diagnosed with left-sided ulcerative colitis 3 years ago and is in clinical remission on sulfasalazine. He and his wife are planning a pregnancy.

What is the best management strategy for this patient?

- A. Continue sulfasalazine
- B. Switch to mesalamine
- C. Switch to budesonide
- D. Switch to azathioprine
- E. Switch to an anti-tumor necrosis factor biologic

CORRECT ANSWER: B

RATIONALE

Sulfasalazine is associated with reversible sperm

dysfunction that can cause male infertility. The best approach in this man seeking to conceive would be to switch to an alternate aminosalicylate such as mesalamine that is not associated with male infertility to treat ulcerative colitis. If sulfasalazine has been effective, it is not necessary to switch to a different class of medication.

REFERENCE

Shin T, Okada H. Infertility in men with inflammatory bowel disease. *World J Gastrointest Pharmacol Ther*. 2016;7(3). doi:10.4292/wjgpt.v7.i3.361

Question 15

A 30-year-old woman with ulcerative colitis is 38 weeks pregnant and is in remission on golimumab. She presents for a routine clinic visit and asks if there are any precautions needed for the baby since she was on anti-tumor necrosis factor (TNF) therapy through her pregnancy.

What is the best advice for this patient regarding her baby?

- A. There are no precautions required
- B. The baby should not receive the rotavirus vaccine in the first 6 months
- C. The baby should not receive DTaP (diphtheria, tetanus, pertussis) vaccine in the first 6 months
- D. The baby should not receive hepatitis B vaccine in the first 6 months
- E. The baby should not receive pneumococcal vaccine in the first 6 months

CORRECT ANSWER: B

RATIONALE

Infants born to mothers on anti-TNF therapy, such as golimumab, will have drug present at birth and should avoid live vaccines during the first 6 months of life. Currently, rotavirus is the only live vaccine recommended in the first 6 months of life and should be held in infants with anti-TNF drugs present in their system.

REFERENCE

McConnell RA, Mahadevan U. Pregnancy and the Patient with Inflammatory Bowel Disease: Fertility, Treatment, Delivery, and Complications. *Gastroenterol Clin North Am.* 2016;45(2). doi:10.1016/j.gtc.2016.02.006

Question 16

A 37-year-old woman with known inflammatory bowel disease is having active symptoms with bloody diarrhea 8 times daily with urgency despite the use of mesalamine. Stool tests are negative for infection. She is initiated on budesonide and a colonoscopy confirms active colitis. Plans are being made to initiate anti-tumor necrosis factor (TNF) therapy.

She is recently married and desires pregnancy in the near future.

Which anti-TNF drug has the least placental transfer and fetal exposure if this patient became pregnant?

- A. Infliximab
- B. Adalimumab
- C. Golimumab
- D. Certolizumab

CORRECT ANSWER: D

RATIONALE

Certolizumab pegol is an anti-TNF drug that does not cross the placenta and is therefore associated with the least fetal exposure. Infliximab, adalimumab, and golimumab are all antibodies that cross the placenta and result in fetal exposure, but they can still be used through pregnancy.

REFERENCE

McConnell RA, Mahadevan U. Pregnancy and the Patient with Inflammatory Bowel Disease: Fertility, Treatment, Delivery, and Complications. *Gastroenterol Clin North Am.* 2016;45(2). doi:10.1016/j.gtc.2016.02.006

Question 17

A 23-year-old woman with stricturing Crohn's disease presents to her gastroenterologist. She was diagnosed with Crohn's ileitis 1 year ago when she was hospitalized for a partial small bowel obstruction. She was initiated on anti-tumor necrosis factor therapy to treat the inflammatory component but has continued to have intermittent episodes of partial small bowel obstruction since then. She was referred to see a surgeon to discuss ileal resection, but before her surgery appointment, she learned that she is pregnant. What is the best management strategy if this patient continues to exhibit signs of obstruction?

- A. Surgery in the first trimester
- B. Surgery in the second trimester
- C. Surgery in the third trimester
- D. Parenteral nutritional support and surgery after delivery

CORRECT ANSWER: B

RATIONALE

When surgery is required during pregnancy, it is generally safest in the second trimester to minimize the risk of spontaneous abortion in the first trimester and the risk of preterm labor in the third trimester. Although there are limited studies on inflammatory bowel disease surgeries during pregnancy, if this patient with stricturing Crohn's disease has recurrent partial small bowel obstructions despite medical therapy, it is likely that she will require surgery during pregnancy.

REFERENCE

Arkenbosch JHC, van Ruler O, de Vries AC. Non-obstetric surgery in pregnancy (including bowel surgery and gallbladder surgery). *Best Pract Res Clin Gastroenterol.* 2020;44-45. doi:10.1016/j.bpg.2020.101669

Question 18

A 27-year-old woman with Crohn's disease and a history of an ileal resection 3 years ago becomes

pregnant. When she presented in the first trimester, she was on no therapy and had active ileitis with a draining perianal fistula. During pregnancy she was treated with steroids and certolizumab, but she continues to have active disease.

What feature of this patient's disease would likely require delivery with a Cesarean section?

- A. Active Crohn's ileitis
- B. Active perianal disease
- C. Active steroid use
- D. Active certolizumab use
- E. Prior Crohn's resection

CORRECT ANSWER: B

RATIONALE

Active perianal disease is an indication for Cesarean section in a woman with Crohn's disease. Outside of active perianal disease, Cesarean sections should be performed for obstetric indications.

REFERENCE

Foulon A, Dupas JL, Sabbagh C, et al. Defining the Most Appropriate Delivery Mode in Women with Inflammatory Bowel Disease: A Systematic Review. *Inflamm Bowel Dis*. 2017;23(5). doi:10.1097/MIB.0000000000001112

Question 19

A 29-year-old woman in her second trimester of pregnancy presents to the emergency department with a 2-day history of melena and hematemesis at the time of presentation. She has no significant medical history and had a hemoglobin of 12.0 g/dL (reference range, 12-16 g/dL) at her last obstetrician appointment 2 weeks ago. Today her heart rate is 135 bpm, and her blood pressure is 105/75 mmHg. Her physical examination is unremarkable other than a gravid uterus. Her hemoglobin is 10.1 g/dL.

After admitting the patient to the hospital and administering intravenous fluids, what is the best management strategy in this patient?

- A. Intravenous famotidine
- B. Intravenous pantoprazole
- C. Intravenous metoclopramide
- D. Urgent upper endoscopy

CORRECT ANSWER: D

RATIONALE

This pregnant patient has signs and symptoms of an active upper gastrointestinal hemorrhage and should be evaluated with an upper endoscopy. Upper endoscopy is the most common endoscopic procedure performed during pregnancy and should be performed when clinically indicated.

REFERENCES

Friedel D. Gastrointestinal endoscopy in the pregnant woman. *World J Gastrointest Endosc*. 2014;6(5). doi:10.4253/wjge.v6.i5.156
 Shergill AK, Ben-Menachem T, Chandrasekhara V, et al. Guidelines for endoscopy in pregnant and lactating women. *Gastrointest Endosc*. 2012;76(1). doi:10.1016/j.gie.2012.02.029

Question 20

A 26-year-old woman is referred by her obstetrician to a gastroenterologist for constipation. She is 21 weeks pregnant. Before pregnancy, she was having 1 formed bowel movement daily. Currently, she is having about 2 bowel movements weekly associated with bloating. There is no blood. Her pregnancy is progressing normally. Her hemoglobin is 12 g/dL (reference range, 12-16 g/dL), her fasting plasma glucose is 75 mg/dL (reference range, 70-99 mg/dL), and her thyroid-stimulating hormone is 1.0 mU/L (reference range, 0.5-4.0 mU/L).

What is the next best step in the management of this patient?

- A. Supplemental fiber
- B. Mineral oil
- C. Lubiprostone
- D. Flexible sigmoidoscopy
- E. Anorectal manometry

CORRECT ANSWER: A**RATIONALE**

Constipation is common in pregnancy and has been associated with thyroid dysfunction and gestational diabetes. In the absence of alarm symptoms, invasive testing is rarely required. Initial therapy should include hydration and supplemental fiber. Other pharmacologic therapy can be used if needed, but mineral oil should be avoided.

REFERENCE

Body C, Christie JA. Gastrointestinal Diseases in Pregnancy. Nausea, Vomiting, Hyperemesis Gravidarum, Gastroesophageal Reflux Disease, Constipation, and Diarrhea. *Gastroenterol Clin North Am.* 2016;45(2). doi:10.1016/j.gtc.2016.02.005

Question 21

A 34-year-old woman presents with a chief complaint of diarrhea. She has a history of diarrhea-predominant irritable bowel syndrome that has been managed with fiber supplementation and loperamide as needed. Her bowels functioned well during her recent pregnancy, and she underwent a Cesarean section for breech presentation 3 weeks ago. For the last week, she reports up to 8 nonbloody bowel movements daily with urgency.

What is the best initial diagnostic test for this patient?

- A. Stool for ova and parasites
- B. Stool for *Clostridioides difficile* toxin
- C. Stool for fecal calprotectin
- D. Serum for tissue transglutaminase antibody
- E. Flexible sigmoidoscopy

CORRECT ANSWER: B**RATIONALE**

Women who have recently undergone Cesarean section have risk factors for *C difficile* infection

including being in a hospital environment and exposure to antibiotics. The initial diagnostic test should be a stool test for *C difficile* toxin. If this is negative, then other diagnoses should be considered.

REFERENCE

Cózar-Llistó A, Ramos-Martinez A, Cobo J. Clostridium difficile Infection in Special High-Risk Populations. *Infect Dis Ther.* 2016;5(3). doi:10.1007/s40121-016-0124-z

Question 22

A 19-year-old woman who is 16 weeks pregnant presents with abdominal pain. She has no significant medical history. She presents with severe abdominal pain in the right lower quadrant that has been present for about 24 hours. She has had some nausea, but no vomiting. She has had no bowel movements in the past 24 hours. She has a temperature of 38.4 °C. Her abdominal examination reveals a gravid uterus and tenderness in the right lower quadrant. Her leukocyte count is 15,100 cells/μL (reference range, 4000–11,000 cells/μL). An abdominal ultrasound reveals an intrauterine pregnancy but is otherwise unremarkable.

What is the next best diagnostic test for this patient?

- A. Stool for *Clostridioides difficile* toxin
- B. Abdominal radiography
- C. Abdominopelvic computed tomography
- D. Abdominopelvic magnetic resonance imaging
- E. Diagnostic laparoscopy

CORRECT ANSWER: D**RATIONALE**

Appendicitis is the most common cause for peritonitis in pregnant woman, present in up to 1 in 500 pregnancies. If there is concern for appendicitis, imaging should be performed. If an ultrasound is nondiagnostic, then magnetic

resonance imaging can evaluate for appendicitis without radiation exposure and is the preferred imaging study.

REFERENCES

Kave M, Parooie F, Salarzaei M. Pregnancy and appendicitis: A systematic review and meta-analysis on the clinical use of MRI in diagnosis of appendicitis in pregnant women. *World J Emerg Surg.* 2019;14(1). doi:10.1186/s13017-019-0254-1

Weinstein MS, Feuerwerker S, Baxter JK. Appendicitis and Cholecystitis in Pregnancy. *Clin Obstet Gynecol.* 2020;63(2). doi:10.1097/GRF.0000000000000529

Question 23

A 35-year-old woman who is 32 weeks pregnant presents to a gastroenterologist due to concern about abnormal laboratory test results obtained during a recent routine visit with her obstetrician. She has a history of anxiety disorder and no other significant medical problems. Her pregnancy is proceeding uneventfully. She reported fatigue to her obstetrician who ordered a series of blood tests, many of which returned outside the normal range. She is currently asymptomatic.

Which of these abnormal lab tests is not routinely affected by pregnancy and might require further evaluation in this patient?

- A. Hematocrit, 32%
- B. Albumin, 3.2 g/dL
- C. Alkaline phosphatase, 165 U/L
- D. Erythrocyte sedimentation rate, 49 mm/hr
- E. Alanine aminotransferase, 52 U/L

CORRECT ANSWER: E

RATIONALE

The alanine aminotransferase level is not typically increased during pregnancy and evaluation should be considered. In normal preg-

nancy, the hematocrit and albumin levels may be decreased, which is associated with volume expansion and the alkaline phosphatase may be increased, which is associated with placental production. Additionally, the erythrocyte sedimentation rate is often increased during pregnancy.

REFERENCE

Abbassi-Ghanavati M, Greer LG, Cunningham FG. Pregnancy and laboratory studies: A reference table for clinicians. *Obstet Gynecol.* 2009;114(6). doi:10.1097/AOG.0bo13e3181c2bde8

Question 24

A 26-year-old woman has a history of left-sided ulcerative colitis for 2 years and has been in clinical and endoscopic remission for 1.5 years. She presents to her gastroenterologist for a routine follow-up visit and reports that she did a home pregnancy test the previous night and it was positive. She has not seen her obstetrician/gynecologist yet and is not on a pre-natal vitamin or folic acid supplement.

Which medicine used to treat ulcerative colitis would require folic acid supplementation in this patient?

- A. Sulfasalazine
- B. Mesalamine
- C. 6-mercaptopurine
- D. Infliximab
- E. Tofacitinib

CORRECT ANSWER: A

RATIONALE

Sulfasalazine alters folic acid metabolism and is often used with folic acid supplementation in the treatment of ulcerative colitis. Deficiency of folic acid during pregnancy is associated with neural tube defects. Although folic acid supplementation may be used in all pregnant patients, it is

necessary in this woman with ulcerative colitis if she is taking sulfasalazine.

REFERENCE

Szymańska E, Kisielewski R, Kierkuś J. Reproduction and Pregnancy in Inflammatory Bowel Disease - Management and Treatment Based on Current Guidelines. *J Gynecol Obstet Hum Reprod*. 2021;50(3). doi:10.1016/j.jogoh.2020.101777

Question 25

A 30-year-old woman with Crohn's disease presents to her gastroenterologist for a routine clinic visit. She has ileocolic disease that is in remission on ustekinumab. She is recently married and is planning pregnancy. Her husband is healthy with no medical problems. She is concerned about the risk of inflammatory bowel disease (IBD) in her offspring.

What is the approximate chance of this patient giving birth to a child with IBD?

- A. 1%
- B. 8%
- C. 22%
- D. 34%
- E. 49%

CORRECT ANSWER: B

RATIONALE

Many chronic medical conditions including IBD are more common in the offspring of parents with that condition. Crohn's disease seems to have some genetic predisposition and studies show that offspring of a parent with Crohn's disease has an increased risk of about 7% to 9 % of being diagnosed with Crohn's disease compared with the general population with a risk lower than 1%.

REFERENCE

Ananthakrishnan AN. Epidemiology and risk factors for IBD. *Nat Rev Gastroenterol Hepatol*. 2015;12(4). doi:10.1038/nrgastro.2015.34

Question 26

A 28-year-old woman with chronic hepatitis B virus (HBV) has been maintained on tenofovir alafenamide for 4 years. Her laboratory evaluation shows that she is HBV surface antigen-positive and HBV e antigen-positive, with alanine aminotransferase (ALT) of 14 U/L (reference range, 10-40 U/L) and HBV DNA that is detectable but level lower than 10 IU/mL.

She tells you she is planning a pregnancy in the near future.

What should you recommend at this time regarding her antiviral treatment in anticipation of pregnancy?

- A. Continue tenofovir alafenamide
- B. Switch to tenofovir disoproxil fumarate
- C. Switch to entecavir
- D. Temporarily discontinue antiviral treatment during pregnancy
- E. Permanently discontinue antiviral treatment

CORRECT ANSWER: B

RATIONALE

Tenofovir disoproxil fumarate is the preferred antiviral agent during pregnancy and breastfeeding due to its safety and high resistance barrier. Tenofovir alafenamide and entecavir have a high resistance barrier but safety during pregnancy has not been demonstrated. Pregnancy is not a reason to discontinue antiviral treatment in women who meet standard criteria for treatment. This patient remains HBV surface antigen-positive and HBV e antigen-positive, so permanent discontinuation of antiviral treatment is not indicated.

REFERENCES

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 27

A 32-year-old woman with chronic hepatitis B virus (HBV) presents for a follow-up visit during her twentieth week of pregnancy. Laboratory evaluation from her previous visit 6 months ago showed that she is HBV surface antigen-positive and HBV e antigen-positive, with alanine aminotransferase (ALT) of 22 U/L (reference range, 10-40 U/L) and HBV DNA of 63,000 IU/mL. Shear wave elastography showed normal liver stiffness. She has never been treated with antiviral medication for HBV.

After checking liver biochemistries and HBV DNA level, what should you recommend regarding HBV management for the remainder of this patient's pregnancy?

- A. There is no need for antiviral treatment if her ALT remains normal
- B. Start antiviral treatment now if her HBV DNA level is >20,000 IU/mL
- C. Start antiviral treatment between week 28 and 32 if her HBV DNA level is >20,000 IU/mL
- D. Start antiviral treatment now if her HBV DNA level is >200,000 IU/mL
- E. Start antiviral treatment between week 28 and 32 if her HBV DNA level is >200,000 IU/mL

CORRECT ANSWER: E

RATIONALE

Antiviral treatment should be instituted during the third trimester to reduce the risk of mother to child transmission in those with a high viral load (>200,000 IU/mL). For women who would not otherwise (ie, outside of pregnancy) require treatment, the decision to start treatment in the third trimester to prevent vertical transmission is based solely on viral load and not on ALT level. This patient has immune-tolerant chronic HBV and initiation of treatment now is not indicated regardless of her viral load.

REFERENCES

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560-1599. doi:10.1002/hep.29800

Question 28

A 25-year-old woman who is 30 weeks pregnant presents to the antepartum triage unit with vomiting, abdominal pain in the right upper quadrant, and confusion. She has no prior history of liver disease.

Her laboratory test results are shown below.

Viral hepatitis serologies are negative. Liver ultrasound shows a small amount of ascites and

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	198	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	81	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	73	10-40
Bilirubin (total), serum, mg/dL	4.5	0.3-1.0
International normalized ratio	1.7	<1.1
Leukocyte count, cells/ μ L	14,000	4000-11,000

no gallstones. After the patient is stabilized, the infant is delivered.

What should the infant be tested for because of his mother’s illness?

- A. Alpha-1 antitrypsin deficiency
- B. Copper (*ATP7b*) gene mutation
- C. Hcpidin gene deficiency
- D. Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency
- E. Alagille (*JAG1*) gene mutation

CORRECT ANSWER: D

RATIONALE

The woman’s presentation is consistent with acute fatty liver of pregnancy. Acute fatty liver of pregnancy may be caused by LCHAD deficiency in the fetus. Therefore, infants born to mothers with acute fatty liver of pregnancy should be tested for LCHAD deficiency. Alpha-1 antitrypsin, hereditary hemochromatosis (hepcidin gene), and Alagille syndrome are causes of chronic liver disease, but do not present with acute liver failure. Wilson disease, from a copper *ATP7b* gene mutation, can present with acute liver failure but when it does so, it is characterized by an alkaline phosphatase to bilirubin ratio lower than 4.

REFERENCES

Frongillo F, Bianco G, Silvestrini N, et al. Acute Liver Failure in an Adult, a Rare Complication of Alagille Syndrome: Case Report and Brief Review. *Transplant Proc.* 2015;47(7):2179-2181. doi:10.1016/j.transproceed.2014.11.072

Korman JD, Volenberg I, Balko J, et al. Screening for Wilson disease in acute liver failure: a comparison of currently available diagnostic tests. *Hepatology.* 2008;48(4):1167-1174. doi:10.1002/hep.22446

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2021;73(1):318-365. doi:10.1002/hep.31559

Question 29

A 36-year-old woman who is 32 weeks pregnant presents to the community hospital emergency department with jaundice and confusion. She has no significant past medical history, and her husband reports that she was in her usual state of health until the day before, when she noticed that she was unusually thirsty and urinating more than usual.

She was disoriented when she woke up on the day of admission, and her husband noticed that her eyes looked a little yellow.

Laboratory evaluation in the emergency department is shown below.

Liver ultrasound shows a bright liver with no signs of hemorrhage. After the infant is emergently delivered, the woman is noted to remain lethargic and confused and international normalized ratio is now 2.1.

What is the next best step for definitive treatment for this patient?

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	213	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	102	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	98	10-40
Bilirubin (total), serum, mg/dL	4	0.3-1.0
Fibrinogen, plasma, mg/dL	77	200-400
International normalized ratio	1.8	<1.1

- A. Administer lactulose orally
- B. Administer lactulose rectally
- C. Transfer to a liver transplantation center
- D. Transfuse fresh frozen plasma
- E. Transfuse cryoprecipitate

CORRECT ANSWER: C

RATIONALE

Her presentation is consistent with acute fatty liver of pregnancy, and she meets criteria for acute liver failure. Therefore, in addition to delivery of the fetus, evaluation for liver transplantation should be pursued. Lactulose, whether given orally or rectally, may help to reduce ammonia levels but is not definitive treatment for acute liver failure. Fresh frozen plasma should be given in acute liver failure only in the setting of active bleeding or a planned invasive procedure. Cryoprecipitate helps to improve fibrinogen levels but is not definitive treatment for acute liver failure.

REFERENCES

Lee WM, Stravitz RT, Larson AM. Introduction to the revised American Association for the Study of Liver Diseases Position Paper on acute liver failure 2011. *Hepatology*. 2012;55(3):965-967. doi:10.1002/hep.25551

Northup PG, Garcia-Pagan JC, Garcia-Tsao G, et al. Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):366-413. doi:10.1002/hep.31646

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guid-

ance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Question 30

A 27-year-old woman whose pregnancy was complicated by pre-eclampsia delivered her baby 1 day ago at 37 weeks. She presents with sudden onset of right upper quadrant abdominal pain. Laboratory evaluation shown below.

Complete blood count shows schistocytes present.

What study should you recommend to evaluate for a complication of this patient's condition?

- A. Upper endoscopy
- B. Hepatobiliary scan
- C. Computed tomography of abdomen with contrast
- D. Serum total bile acid level
- E. Gastric emptying study

CORRECT ANSWER: C

RATIONALE

This patient's presentation is consistent with postpartum HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelet count) syndrome, evidenced by abnormal liver biochemistries, low platelets, and findings of hemolysis (in this case, the presence of schistocytes). Pre-eclampsia is commonly in patients with HELLP syndrome, as pre-eclampsia, eclampsia, and HELLP syndrome are all on the spectrum of hypertensive disease of pregnancy. Patients with HELLP syndrome are at risk for hepatic infarct, hemorrhage, and rupture, which may present with abdominal or shoulder

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	514	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	624	10-40
Bilirubin (total), serum, mg/dL	3	0.3-1.0
Platelet count, <i>plts</i> /μL	75,000	150,000-450,000

pain or hypotension. If any of these signs are present, imaging of the abdomen should be performed. For this patient, a computed tomography of the abdomen with contrast would be the best study to evaluate for this complication; none of the other listed studies assess for complications of HELLP syndrome.

REFERENCE

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Question 31

A 38-year-old woman in her 34th week of pregnancy presents to the antepartum unit with nausea and vomiting. Her blood pressure is 152/96 mmHg. Her laboratory test results are shown below.

Her complete blood count with differential shows the presence of spherocytes. Her mental status is normal.

What intervention should you recommend for definitive treatment of this patient’s condition?

- A. Urgent liver transplant evaluation
- B. Delivery
- C. N-acetylcysteine
- D. Labetalol
- E. Platelet transfusion

CORRECT ANSWER: B

RATIONALE

Her presentation is consistent with HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelet count) syndrome, which commonly presents with abdominal pain, nausea, and vomiting. She has evidence of elevated liver biochemistries, thrombocytopenia, and hemolysis (evidenced by spherocytes seen on her complete blood count with differential). She is also hypertensive; pre-eclampsia is a commonly seen in patients with HELLP syndrome, and HELLP syndrome is also more common in those with preexisting hypertension. Patients with HELLP syndrome should undergo expeditious delivery. Neither urgent liver transplant evaluation nor N-acetylcysteine is indicated at this point as she is not in acute liver failure. Labetalol is appropriate for treatment of hypertension in pregnancy but is not definitive treatment for HELLP syndrome. Platelet transfusion may be appropriate if she has bleeding or undergoes an invasive procedure but it, too, is not definitive treatment for HELLP syndrome.

REFERENCES

Northup PG, Garcia-Pagan JC, Garcia-Tsao G, et al. Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):366-413. doi:10.1002/hep.31646

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	593	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	542	10-40
Bilirubin (total), serum, mg/dL	2.1	0.3-1.0
International normalized ratio (INR)	0.98	<1.1
Platelet count, plts/ μ L	48,000	150,000-450,000

Question 32

A 30-year-old woman in her eleventh week of pregnancy is admitted with intractable nausea and vomiting. Alanine aminotransferase is 93 U/L (reference range, 10–40 U/L), aspartate aminotransferase is 74 U/L (reference range, 10–40 U/L), and bilirubin is normal. Her liver ultrasound is normal.

In addition to giving antiemetics and intravenous fluids, which of the following should you recommend to prevent a complication of this patient's condition?

- A. Vitamin K
- B. Albumin
- C. Iron supplement
- D. Thiamine
- E. Folate

CORRECT ANSWER: D

RATIONALE

This clinical presentation is characteristic of hyperemesis gravidarum, which commonly presents in the first trimester with elevated transaminases in the setting of intractable nausea and vomiting. Women with hyperemesis gravidarum are at risk for Wernicke's encephalopathy, a neuropsychiatric syndrome associated with acute thiamine deficiency, as pregnancy increases thiamine requirements, and vomiting and lack of dietary intake decrease thiamine supplies. Wernicke's encephalopathy is characterized by ataxia, oculomotor dysfunction, and altered mental status. Thiamine should be administered to patients with hyperemesis gravidarum to prevent Wernicke's encephalopathy.

None of the other interventions listed are used to treat complications of hyperemesis gravidarum.

REFERENCES

Oudman E, Wijnia JW, Oey M, van Dam M, Painter RC, Postma A. Wernicke's encephalopathy in hyperemesis gravidarum: A systematic review. *Eur J Obstet Gynecol Reprod Biol.* 2019;236:84–93. doi:10.1016/j.ejogrb.2019.03.006

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2021;73(1):318–365. doi:10.1002/hep.31559

Question 33

A 23-year-old woman who is 10 weeks pregnant is hospitalized with nausea, vomiting, and weight loss. With supportive care, her symptoms improve; on hospital day 4, she is tolerating an oral diet and not requiring antiemetics. Laboratory evaluation done at admission and on day 4 shows the following results shown below.

What should you advise regarding a laboratory and imaging evaluation for causes of elevated liver enzymes in this patient?

- A. No further testing is needed since her symptoms have resolved
- B. She should have further testing since her liver biochemistries remain elevated after her symptoms have resolved
- C. She should have further testing if her liver biochemistries remain elevated after 1–2 months

Laboratory Test	Results at admission	Results on Day 4	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	98	102	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	104	93	10–40
Bilirubin (total), serum, mg/dL	1.4	1.5	0.3–1.0

- D. She should have further testing if her liver biochemistries remain elevated in the third trimester
- E. She should have further testing if her liver biochemistries remain elevated after delivery

CORRECT ANSWER: B

RATIONALE

This patient's presentation is suggestive of hyperemesis gravidarum, as she is in her first trimester and has intractable nausea and vomiting resulting in weight loss and the need for hospitalization. However, the liver test abnormalities associated with hyperemesis gravidarum are expected to resolve with resolution of symptoms; if they do not, as in this case, other causes should be sought.

REFERENCE

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Question 34

A 35-year-old woman has a computed tomography for kidney stones, and she is incidentally found to have a 7 cm liver lesion. Further evaluation with magnetic resonance imaging shows this to be a hepatic adenoma with no signs of hemorrhage.

She reports that she is using a copper intrauterine device (IUD) for contraception but plans to have it removed within the next year so that she can try to conceive.

What would be the best recommendation at this point regarding management of this patient's adenoma?

- A. No treatment or surveillance since it is benign
- B. Surveillance imaging every 6-12 months with no change in management if she becomes pregnant

- C. Surveillance imaging every 6-12 months and continue contraception as pregnancy is contraindicated
- D. Surveillance imaging during pregnancy and plan for embolization or resection of the adenoma after delivery
- E. Embolization or resection of the adenoma before pregnancy

CORRECT ANSWER: E

RATIONALE

Hepatic adenomas are benign liver lesions with the potential to be complicated by hemorrhage or progression to hepatocellular carcinoma. In nonpregnant women, small (<5 cm) hepatic adenomas warrant imaging surveillance every 6 to 12 months, and resection or embolization should be considered for hepatic adenomas larger than 5 cm, owing to their higher risk of complications. Because the growth of hepatic adenomas is promoted by sex hormones, appropriate management of large adenomas before pregnancy is particularly important. Answer A is incorrect because all hepatic adenomas warrant surveillance or treatment, even though they are benign. Because this patient's adenoma is larger than 5 cm, surveillance is not the best management option regardless of pregnancy plans. Large adenomas should be treated before pregnancy, due to the potential for growth and complications during pregnancy.

REFERENCES

Marrero JA, Ahn J, Rajender Reddy K; American College of Gastroenterology. ACG clinical guideline: the diagnosis and management of focal liver lesions. *Am J Gastroenterol*. 2014;109(9):1328-1348. doi:10.1038/ajg.2014.213

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Question 35

A 28-year-old woman is followed in your hepatology clinic for hepatic adenomatosis. She has at least 12 hepatic adenomas, the largest of which is 3 cm. She has had surveillance imaging showing no change in the size of the lesions over the last 4 years. She does not use hormonal contraception. She calls the office to notify you that she is now 6 weeks pregnant.

What should you recommend for management of hepatic adenomatosis in this patient?

- A. Magnetic resonance imaging (MRI) with contrast now and in 6 months
- B. MRI with contrast once per trimester, and 3 months after delivery
- C. Ultrasound now and in 6 months
- D. Ultrasound once per trimester and 3 months after delivery
- E. Defer further imaging until after delivery

CORRECT ANSWER: D

RATIONALE

Because of the potential for growth of hepatic adenomas during pregnancy, pregnant patients with hepatic adenomas should be monitored with ultrasound once per trimester and 12 weeks after delivery. Although MRI with contrast is useful for diagnosis and surveillance of hepatic adenomas in nonpregnant patients, it should be avoided in pregnancy since gadolinium crosses the placenta.

REFERENCES

Committee Opinion No. 723: Guidelines for Diagnostic Imaging During Pregnancy and Lactation. *Obstet Gynecol.* 2017;130(4):e210-e216. doi:10.1097/AOG.0000000000002355

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2021;73(1):318-365. doi:10.1002/hep.31559

Question 36

A 35-year-old woman with alcohol-related cirrhosis comes to see you in clinic in her 12th week of pregnancy. She has not consumed any alcohol in 4 years. She is not currently taking any medications. Her most recent upper endoscopy was 2 years ago and demonstrated no esophageal varices.

Her laboratory tests show the following results displayed below.

What is the best recommendation regarding a follow-up endoscopy in this patient to screen for esophageal varices?

- A. She should have an endoscopy in 1 year
- B. She should have an endoscopy as soon as possible
- C. She should have an endoscopy early in her second trimester
- D. She should have an endoscopy early in her third trimester
- E. She does not need to have another endoscopy unless she develops symptoms

CORRECT ANSWER: C

RATIONALE

There is increased risk of variceal bleeding during pregnancy and delivery, related to increased maternal blood volume and compression of blood vessels within the abdomen. Thus, pregnant

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	593	10–40
Bilirubin (total), serum, mg/dL	0.9	0.3–1.0
International normalized ratio (INR)	1.02	<1.1
Platelet count, plts/ μ L	143,000	150,000–450,000

patients with cirrhosis should have an endoscopy early in the second trimester to screen for varices if they have not had one within 1 year, unless they are already taking a beta blocker for primary prophylaxis.

REFERENCES

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Shaheen AA, Myers RP. The outcomes of pregnancy in patients with cirrhosis: a population-based study. *Liver Int*. 2010;30(2):275-283. doi:10.1111/j.1478-3231.2009.02153.x

Question 37

A 28-year-old woman with cirrhosis secondary to autoimmune hepatitis plans to try and conceive. She has never had a variceal hemorrhage but had an endoscopy 2 years ago that demonstrated Grade 2 esophageal varices.

She is maintained on carvedilol for primary prophylaxis. On treatment, her blood pressure is 102/84 mmHg, and her heart rate is 72 bpm.

What should you counsel this patient regarding prophylaxis of variceal bleeding during pregnancy?

- A. She should continue carvedilol at her current dose during pregnancy
- B. She should take a higher dose of carvedilol during pregnancy
- C. She should take nadolol instead of carvedilol during pregnancy
- D. She should take propranolol instead of carvedilol during pregnancy
- E. She should not take any nonselective beta blocker during pregnancy

CORRECT ANSWER: D

RATIONALE

Although nadolol, propranolol, and carvedilol are all appropriate options for primary prophylaxis of variceal bleeding in non-pregnant patients, propranolol is the preferred agent for prophylaxis of variceal bleeding during pregnancy. Carvedilol is not the preferred agent during pregnancy due to a lack of safety data. Although nadolol and propranolol are both associated with some degree of risk to the fetus, nadolol is not the preferred agent due to its longer half-life and decreased protein binding, which may prolong the risk of neonatal complications.

REFERENCES

Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology*. 2017;65(1):310-335. doi:10.1002/hep.28906

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Welzel T, Donner B, van den Anker JN. Intrauterine Growth Retardation in Pregnant Women with Long QT Syndrome Treated with Beta-Receptor Blockers. *Neonatology*. 2021;118(4):406-415. doi:10.1159/000516845

Question 38

A 20-year-old woman with autoimmune hepatitis presents for a follow-up appointment. She is 8 weeks pregnant. She was diagnosed with autoimmune hepatitis 3 years ago and is currently maintained on azathioprine 50 mg daily. Her liver biochemistries are normal, and they have been for the last 18 months. She is asymptomatic.

What should you counsel this patient about the risk of a postpartum flare of her disease?

- A. Pregnancy and the postpartum period are not associated with any changes in autoimmune hepatitis disease activity
- B. The risk of a postpartum flare is the same as the risk of a flare during pregnancy
- C. The risk of a postpartum flare is lower than the risk of a flare during pregnancy
- D. Continuing immunosuppression during pregnancy increases the risk of a postpartum flare
- E. 1 year of remission before conception decreases the risk of a postpartum flare

CORRECT ANSWER: E

RATIONALE

Patients whose autoimmune hepatitis was in remission for more than 1 year before conception have a lower risk of a postpartum flare. Pregnancy and the postpartum period are associated with changes in disease activity in autoimmune hepatitis; liver biochemistries tend to improve during pregnancy, and the risk of a disease flare is highest after childbirth. Use of immunosuppression during pregnancy is associated with a lower risk of a postpartum flare.

REFERENCES

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Westbrook RH, Yeoman AD, Kriese S, Heneghan MA. Outcomes of pregnancy in women with autoimmune hepatitis. *J Autoimmun*. 2012;38(2-3):J239-J244. doi:10.1016/j.jaut.2011.12.002

Question 39

A 33-year-old woman with autoimmune hepatitis presents to establish care. She was diagnosed with autoimmune hepatitis 8 years ago when she presented with jaundice. She was initially treated with prednisone and azathioprine, but discon-

tinued azathioprine due to pancreatitis and was started on mycophenolate mofetil instead. She is currently taking mycophenolate mofetil monotherapy and has normal liver biochemistries.

She is using an intrauterine device for contraception but plans to have it removed so she can try to conceive.

What should you counsel this patient regarding the treatment for autoimmune hepatitis in anticipation of pregnancy?

- A. Continue mycophenolate while trying to conceive and throughout pregnancy
- B. Continue mycophenolate until she becomes pregnant, then discontinue treatment during pregnancy
- C. Continue mycophenolate until she becomes pregnant, then switch to an alternative agent
- D. Stop mycophenolate at least 6 weeks before trying to conceive
- E. Stop mycophenolate at least 6 months before trying to conceive

CORRECT ANSWER: D

RATIONALE

Use of mycophenolate (mycophenolic acid or mycophenolate mofetil) during pregnancy is contraindicated due to the risk of miscarriage congenital malformations. Mycophenolate should be discontinued at least 6 weeks before conception.

REFERENCES

Kim M, Rostas S, Gabardi S. Mycophenolate fetal toxicity and risk evaluation and mitigation strategies. *Am J Transplant*. 2013;13(6):1383-1389. doi:10.1111/ajt.12238

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Question 40

A 38-year-old woman presents with a liver lesion. A liver ultrasound 6 months ago to evaluate right upper quadrant abdominal pain showed a 1.2 cm hyperechoic liver lesion. The patient was referred to the hepatology clinic, but has missed several appointments; today, she tells you that she is 20 weeks pregnant.

What would be most accurate counseling for this patient regarding the imaging of her liver during pregnancy?

- A. No liver imaging is safe during pregnancy
- B. There is minimal risk from computed tomography (CT) radiation before 25 weeks
- C. There is minimal risk from CT radiation after 25 weeks
- D. Nonionic contrast for CT is associated with a risk of neonatal hypothyroidism
- E. Gadolinium contrast for magnetic resonance imaging does not cross the placenta

CORRECT ANSWER: C

RATIONALE

The liver can be imaged safely during pregnancy. There is minimal risk from radiation after 25 weeks; radiation may be teratogenic up to the eighth week of pregnancy and is associated with cognitive risk to the fetus at up to 25 weeks of pregnancy. Only iodinated CT contrast is associated with neonatal hypothyroidism. Gadolinium contrast crossed the placenta and should not be used during pregnancy.

REFERENCES

Committee Opinion No. 723: Guidelines for Diagnostic Imaging During Pregnancy and Lacta-

tion. *Obstet Gynecol.* 2017;130(4):e210-e216. doi:10.1097/AOG.0000000000002355

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Question 41

A 21-year-old woman with chronic hepatitis C virus (HCV) is referred to see you in her twentieth week of pregnancy. She is treatment naive. Recent laboratory evaluation is shown below.

Her HCV RNA is 485,000 IU/mL. What should you counsel her regarding reducing the risk of mother to child transmission of HCV?

- A. She should deliver via Caesarian section
- B. She should deliver vaginally
- C. Mode of delivery does not affect the risk of mother to child transmission
- D. She should immediately start treatment with direct-acting antivirals (DAAs)
- E. She should start treatment with DAAs between the weeks of 28 and-32 of the pregnancy

CORRECT ANSWER: C

RATIONALE

Mode of delivery does not affect the risk of vertical transmission of hepatitis C virus. DAAs should not be used during pregnancy as safety during pregnancy has not been established.

REFERENCES

Hughes BL, Page CM, Kuller JA. Hepatitis C in

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	84	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	78	10-40
Bilirubin (total), serum, mg/dL	0.9	0.3-1.0

pregnancy: screening, treatment, and management. *Am J Obstet Gynecol.* 2017;217(5):B2-B12. doi:10.1016/j.ajog.2017.07.039

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Question 42

A 35-year-old man with decompensated cirrhosis comes to see you for treatment of hepatitis C virus (HCV). He has no history of prior treatment. He has HCV genotype 1b, and his HCV RNA level is 138,000 IU/mL. Laboratory evaluation shows a hemoglobin level of 12 mg/dL (reference range, 14-18 mg/dL) and platelet count of 138,000 plts/ μ L (reference range, 150,000-450,000 plts/ μ L).

You agree upon a treatment regimen including a direct-acting antiviral (DAA) and ribavirin. He mentions that he and his wife are hoping to have another child.

What should you counsel him regarding his anticipated course of treatment?

- A. Conception plans are irrelevant to HCV treatment in men
- B. Conception should be deferred until at least 6 months after treatment due to the teratogenicity of DAAs
- C. Conception should be deferred until at least 6 months after treatment due to the teratogenicity of ribavirin
- D. Conception should be deferred until at least 6 weeks after treatment due to the teratogenicity of DAAs
- E. Conception should be deferred until at least 6 weeks after treatment due to the teratogenicity of ribavirin

CORRECT ANSWER: C

RATIONALE

Ribavirin is teratogenic in men as well as women; for either, conception should be deferred until at least 6 months after completing treatment with ribavirin. DAA use by men has no known association with fetal risk.

REFERENCE

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2021;73(1):318-365. doi:10.1002/hep.31559

Question 43

A 38-year-old woman presents for a routine follow-up visit for primary biliary cholangitis (PBC). She was diagnosed with PBC 5 years ago, based on a positive antimitochondrial antibody and a liver biopsy showing florid duct lesions. She is maintained on ursodiol with an excellent biochemical response. She is now 10 weeks pregnant.

Which of the following should you include in her laboratory evaluation today to inform management later in this patient's pregnancy?

- A. Alkaline phosphatase isoenzymes
- B. Anti-mitochondrial antibody
- C. Heat-fractionated alkaline phosphatase
- D. Serum total bile acids
- E. Quantitative IgM

CORRECT ANSWER: D

RATIONALE

In patients with PBC, measuring total bile acids in the first trimester can help establish a baseline of what bile acid level is normal for the patient to determine whether there is intrahepatic cholestasis of pregnancy later. Alkaline phosphatase isoenzymes and heat-fractionated alkaline phosphatase are helpful in determining whether elevated alkaline phosphatase is due to a liver source but measuring this in early pregnancy is unlikely to

impact management later in pregnancy. Similarly, an elevated IgM level supports the diagnosis of PBC but measurement in a patient with known PBC is unlikely to change management during pregnancy.

REFERENCE

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

Question 44

A 28-year-old woman with primary biliary cholangitis (PBC) inquires about management of PBC if she becomes pregnant. She was diagnosed with PBC 2 years ago. She was initially treated with ursodiol, but experienced thinning hair as a side effect and switched to obeticholic acid. She has had a good biochemical response to obeticholic acid and has a normal alkaline phosphatase level.

What should you counsel this patient regarding treatment during pregnancy?

- A. Obeticholic acid, but not ursodiol, has evidence of safety during pregnancy
- B. Ursodiol, but not obeticholic acid, has evidence of safety during pregnancy
- C. Both obeticholic acid and ursodiol have evidence of safety during pregnancy
- D. Both obeticholic acid and ursodiol have been proven to be unsafe for use during pregnancy
- E. There is no data regarding the safety of either obeticholic acid or ursodiol during pregnancy

CORRECT ANSWER: B

RATIONALE

Ursodiol is safe during pregnancy, but the safety of obeticholic acid during pregnancy has not yet been established.

REFERENCE

Efe C, Kahramanoğlu-Aksoy E, Yilmaz B, et al. Pregnancy in women with primary biliary cirrhosis. *Autoimmun Rev*. 2014;13(9):931-935. doi:10.1016/j.autrev.2014.05.008

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Question 45

A 28-year-old woman is admitted to the hospital with nausea in her third trimester of pregnancy and is found to have markedly elevated liver enzymes. Liver ultrasound is normal. Serologic evaluation for hepatitis A, B, and C are negative, as are autoimmune serologies. Her blood pressure, international normalized ratio, and platelet count are normal. Her liver enzymes gradually improve with supportive care, and hepatitis E IgM is found to be positive.

How should you counsel this patient about hepatitis E in pregnancy?

- A. The hepatitis E IgM is probably a false positive, as people are less susceptible to hepatitis E during pregnancy
- B. Severe hepatitis E infections occur less commonly in pregnant patients than in nonpregnant patients
- C. Maternal hepatitis E infection is not associated with a risk of adverse pregnancy outcomes
- D. Mother to child transmission of hepatitis E does not occur
- E. Mother to child transmission of hepatitis E can occur

CORRECT ANSWER: E

RATIONALE

Pregnancy is associated with greater susceptibility to hepatitis E and with more severe outcomes. Ma-

ternal hepatitis E infections confers a risk of fetal loss. Mother to child transmission of hepatitis E occurs in 33% to 100% of cases.

REFERENCES

Li M, Bu Q, Gong W, et al. Hepatitis E virus infection and its associated adverse fetomaternal outcomes among pregnant women in Qinhuangdao, China. *J Matern Fetal Neonatal Med.* 2020; 33(21):3647-3651. doi:10.1080/14767058.2019.1582630

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Question 46

A 19-year-old woman in the second trimester of pregnancy presents with fever and mild confusion. She has no rashes on her skin. Her laboratory test results are shown below.

Ultrasound reveals a normal liver and no evidence of cholecystitis. Blood and urine cultures are negative. A hepatitis panel shows no evidence of acute hepatitis A or B; Epstein-Barr virus polymerase chain reaction (PCR) and cytomegalovirus (CMV) PCR tests are both negative.

What medication should be started empirically for this patient while awaiting additional diagnostic results?

- A. Intravenous (IV) N-acetylcysteine
- B. IV acyclovir

- C. Oral acyclovir
- D. IV ganciclovir
- E. Oral ganciclovir

CORRECT ANSWER: B

RATIONALE

Herpes simplex virus (HSV) hepatitis should be suspected in a pregnant patient with fever and liver enzymes in the thousands that are otherwise unexplained. Due to the severe morbidity and mortality, empiric treatment with IV acyclovir should be started without delay (while awaiting additional diagnostic results such as HSV PCR) if HSV hepatitis is suspected. N-acetylcysteine is not indicated as this patient does not have liver failure (normal INR). Ganciclovir would be used to treat CMV, for which the patient tested negative.

REFERENCES

Kang AH, Graves CR. Herpes simplex hepatitis in pregnancy: a case report and review of the literature. *Obstet Gynecol Surv.* 1999;54(7):463-468. doi:10.1097/00006254-199907000-00026

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Question 47

A 39-year-old woman who is in the twenty-eighth week of her fourth pregnancy is referred to you for evaluation of elevated liver enzymes.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	238	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	3,006	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	2,130	10-40
Bilirubin (total), serum, mg/dL	2	0.3-1.0
International normalized ratio (INR)	1	<1.1
Platelet count, <i>plts</i> /μL	130,000	150,000-450,000

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	168	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	127	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	103	10-40
Bilirubin (total), serum, mg/dL	1.2	0.3-1.0

She initially presented to her obstetrician with pruritis and was found to have the following laboratory test results are shown above.

Liver biochemistries before pregnancy were all within normal limits, and recent viral hepatitis panel and autoimmune serologies are all negative.

What finding on further diagnostic testing would confirm the diagnosis of intrahepatic cholestasis of pregnancy (ICP)?

- A. Mild intrahepatic biliary ductal dilation on ultrasound
- B. Serum total bile acids of 8 μmol/L
- C. Serum total bile acids of 18 μmol/L
- D. Normal heat-stable alkaline phosphatase
- E. Normal 5'-nucleotidase

CORRECT ANSWER: C

RATIONALE

In the absence of other causes, a serum total bile acid level higher than 10 μmol/L in a pregnant patient with pruritis is consistent with ICP. ICP is not associated with biliary ductal dilation. Laboratory tests aimed at determining whether alkaline phosphatase is elevated due to a liver problem (heat-fractionated alkaline phosphatase and 5'-nucleotidase) do not play a role in the diagnosis of ICP.

REFERENCES

Bicocca MJ, Sperling JD, Chauhan SP. Intrahepatic cholestasis of pregnancy: Review of six national and regional guidelines. *Eur J Obstet Gynecol Reprod Biol.* 2018;231:180-187. doi:10.1016/j.ejogrb.2018.10.041

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ance by the American Association for the Study of Liver Diseases. *Hepatology.* 2021;73(1):318-365. doi:10.1002/hep.31559

Question 48

A 35-year-old woman with diabetes and obesity presents with severe pruritis in the third trimester of pregnancy. Liver enzymes are normal, and serum total bile acid level is 45 μmol/L. Prothrombin time is normal. She has no family history of intrahepatic cholestasis of pregnancy (ICP). She did not have pruritis during her prior pregnancy.

What would be the most appropriate recommendation at this time for this patient?

- A. Start ursodiol 10-15 mg/kg
- B. Start ursodiol 13-15 mg/kg
- C. Start vitamin K supplements
- D. Test for genetic variants associated with cholestasis
- E. No changes in the timing of her delivery

CORRECT ANSWER: A

RATIONALE

ICP is treated with ursodiol 10 to 15 mg/kg; 13 to 15 mg/kg is the dose used for primary biliary cholangitis. Vitamin K only needs to be supplemented if the prothrombin time is prolonged. Testing for genetic variants associated with cholestasis is indicated in early or recurrent ICP and those with bile acid level higher than 100 μmol/L. ACOG recommends that women with ICP deliver at 36 to 37 weeks.

REFERENCES

ACOG Committee Opinion No. 764: Medically Indicated Late-Preterm and Early-Term Deliv-

eries. *Obstet Gynecol.* 2019;133(2):e151-e155. doi:10.1097/AOG.0000000000003083

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Question 49

A 24-year-old woman returns for follow-up after liver transplantation. She underwent a transplant at the age of 17 for acute liver failure secondary to acetaminophen overdose. She had an episode of acute rejection in the early post-transplantation period, but she has had stable graft function for 2 years. She is maintained on tacrolimus 1 mg twice daily with a recent trough level of 3.5. She informs you that she plans to start trying to conceive.

What should you counsel this patient regarding her immunosuppression?

- A. She should stop tacrolimus and switch to prednisone before conception
- B. She should stop tacrolimus and switch to everolimus before conception
- C. She should stop tacrolimus and switch to azathioprine before conception
- D. She should discontinue tacrolimus as soon as she has a positive pregnancy test
- E. She should make no changes in her immunosuppression at this time

CORRECT ANSWER: E

RATIONALE

Tacrolimus is safe during pregnancy, so there is no need to switch to prednisone or azathioprine or to discontinue tacrolimus after becoming pregnant. Everolimus should not be used during pregnancy.

REFERENCES

McKay DB, Josephson MA, Armenti VT, et al. Reproduction and transplantation: report on

the AST Consensus Conference on Reproductive Issues and Transplantation. *Am J Transplant.* 2005;5(7):1592-1599. doi:10.1111/j.1600-6143.2005.00969.x

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2021;73(1):318-365. doi:10.1002/hep.31559

Question 50

A 30-year-old woman returns for follow-up after liver transplantation. She underwent a transplant 2 years ago for cirrhosis secondary to autoimmune hepatitis. Her post-transplant course has been uneventful, and her liver biochemistries have all been within normal limits for the last year on stable doses of tacrolimus 2 mg twice daily and prednisone 5 mg daily. She currently uses a copper intrauterine device for contraception but would like to have a child and asks what you recommend with regard to pregnancy after liver transplantation.

What would be the most appropriate recommendation for this patient?

- A. Liver transplant recipients should not become pregnant
- B. Tacrolimus trough levels should be monitored every 2-4 weeks if she becomes pregnant
- C. No change to her tacrolimus monitoring is needed if she becomes pregnant
- D. Pregnancy can be considered 1 year or more after liver transplantation, but maternal mortality is significantly higher compared with the general population
- E. Pregnancy can be considered 1 year or more after liver transplantation, but fetal/neonatal survival is significantly lower compared with the general population

CORRECT ANSWER: B

RATIONALE

The American Transplant Society suggests that liver transplant recipients wait at least 2 years after transplant before becoming pregnant. Tacrolimus trough levels should be monitored every 2 to 4 weeks during pregnancy. Maternal and fetal/neonatal survival do not differ significantly between liver transplant recipients and the general population.

REFERENCES

McKay DB, Josephson MA, Armenti VT, et al. Reproduction and transplantation: report on the AST Consensus Conference on Reproductive Issues and Transplantation. *Am J Transplant*. 2005;5(7):1592-1599. doi:10.1111/j.1600-6143.2005.00969.x

Sarkar M, Brady CW, Fleckenstein J, et al. Reproductive Health and Liver Disease: Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;73(1):318-365. doi:10.1002/hep.31559

CHAPTER 9

Diarrhea and constipation

Stacy Menees, MD and Brandon Sprung, MD

Question 1

A 34-year-old woman is being seen by her primary care provider. She reports a history of intermittent abdominal pain that has been going on for at least a year and is improved with defecation. When asked about her bowel habits, she reports that it is often “hard for her to go,” which happens at least 2 to 3 times weekly. The primary care provider determines that the patient has a type 1 stool on the Bristol Stool Scale. The patient has not previously sought treatment for these complaints, and this is the first time she has talked about it with a provider.

What treatment is most likely to improve her abdominal pain and constipation?

- A. Hyoscyamine
- B. *Lactobacillus*
- C. Psyllium
- D. Polyethylene glycol

CORRECT ANSWER: C**RATIONALE**

This patient meets the Rome IV criteria for irritable bowel syndrome with constipation (IBS-C), given that she has abdominal discomfort associated with a change in the form of stool, and the discomfort is related to defecation. As per the most recent American College of Gastroenterology guidelines, the first step in treatment of a patient with IBS-C would be the use of soluble fiber to treat global IBS symptoms. This is a strong recommendation, with a moderate quality

of evidence. The use of a soluble, viscous, poorly fermentable fiber may provide benefits in IBS. The lack of significant side effects makes fiber a reasonable first-line therapy. Soluble fiber can improve stool viscosity and frequency, which supports the use of fiber in patients with IBS-C. The guidelines recommend against the use of antispasmodics or probiotics to treat global IBS symptoms. Although polyethylene glycol is very effective for treatment of constipation, its efficacy for IBS-C has not been supported, because randomized controlled trials have failed to show that polyethylene glycol improves either overall symptoms or pain in patients with IBS-C.

REFERENCE

Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036

Question 2

Which statement represents the physiology of a normal bowel movement?

- A. Each day, approximately 1000 mL of fluid enters the cecum from the terminal ileum where 75% of the salt and water is reabsorbed
- B. Each day, approximately 1500 mL of fluid enters the cecum from the terminal ileum where 95% of the salt and water is reabsorbed

- C. Each day, approximately 3000 mL of fluid enters the cecum from the terminal ileum where 80% of the salt and water is reabsorbed
- D. Each day, approximately 4000 mL of fluid enters the cecum from the terminal ileum where 90% of the salt and water is reabsorbed

CORRECT ANSWER: B

RATIONALE

Each day, approximately 1500 mL of fluid enters the cecum from the terminal ileum. This fluid is composed of the residues of the digestive process, which is mostly salt, water, and fiber (indigestible carbohydrate). Transit through the colon is slow, taking 24 to 30 hours for material to pass from the cecum to the rectum. During this time, 95% of the salt and water is reabsorbed and much of the fiber is fermented into gas and short-chain fatty acids by colonic bacteria. These products are absorbed by the colonic mucosa and the amount of feces produced is only a small fraction of what entered the colon (about 80-120 g/24 hours).

REFERENCE

Venkatasubramanian J, Rao MC, Sellin JH. Intestinal Electrolyte Absorption and Secretion. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*, 10th ed. Elsevier, Inc; 2016:1675-1694.

Question 3

A 48-year-old woman with a history of hypertension is being seen by her primary care provider. She reports a change in her bowel habits with infrequent, hard stools since sometime in the last year. She did start an antihypertensive medication 6 months ago. What is the best next step in the care of this patient?

- A. Stop antihypertensive medication
- B. Prescribe psyllium
- C. Start *Lactobacillus*
- D. Perform colonoscopy

CORRECT ANSWER: D

RATIONALE

Colonoscopy should be done to exclude malignancy in patients 45 years of age or older who present with constipation for the first time. Although the new medication is likely the culprit for her symptoms, all patients over screening age with new-onset change in bowel habits should undergo a colonoscopy first. Psyllium can be used for constipation, but a colonoscopy is needed first to rule out a structural cause in someone over 45 with new-onset constipation. *Lactobacillus* or other probiotics are not effective for treatment of constipation.

REFERENCE

Bharucha AE, Pemberton JH, Locke GR 3rd. American Gastroenterological Association technical review on constipation. *Gastroenterology*. 2013;144(1):218-238. doi:10.1053/j.gastro.2012.10.028

Question 4

A 28-year-old woman with no significant past medical history is being seen by a gastroenterologist due to “years of constipation.” She denies any abdominal pain but has a problem with “going to the bathroom.” She has a bowel movement every 4 to 5 days. She has tried all types of fiber without alleviation of her symptoms. Which of the following findings on physical examination would change the management strategy?

- A. Tenderness to palpation in the left lower quadrant
- B. Intact anal wink
- C. Decreased anal sphincter tone
- D. Paradoxical contraction of puborectalis with straining

CORRECT ANSWER: D

RATIONALE

Functional outlet obstruction, or dyssynergic defecation, coexists with slow transit in approximately 20% to 25% of patients presenting to gastroen-

terologists for evaluation of difficult constipation. This should be assessed with a digital rectal examination, in which the patient is asked to expel the examining finger. Paradoxical contraction of the sphincter or puborectalis during straining is suggestive of dyssynergic defecation, which can be formally diagnosed with anorectal manometry. Treatment for this condition includes biofeedback, rather than laxatives alone.

REFERENCE

Bharucha AE, Pemberton JH, Locke GR 3rd. American Gastroenterological Association technical review on constipation. *Gastroenterology*. 2013;144(1):218-238. doi:10.1053/j.gastro.2012.10.028

Question 5

A 36-year-old man presents to the emergency department. He has a long history of recurrent episodes of constipation and abdominal distention since early adulthood. He now has abdominal pain and severe vomiting. Vital signs: blood pressure, 110/64 mmHg; heart rate, 110 bpm; temperature, 36.8 °C; oxygen saturation, 98%. His abdominal examination shows a distended abdomen without guarding or rebound. Digital rectal examination revealed elevated anal sphincteric tone with a high rectal fecal load. Routine laboratory evaluation, including a complete blood count, urinalysis, and blood chemistry testing, are all within normal limits.

Which of the following tests is most likely to establish the diagnosis?

- A. Deep rectal biopsy
- B. Abdominal computer tomography
- C. Barium enema
- D. Colonoscopy

CORRECT ANSWER: A

RATIONALE

This is a case of Hirschsprung disease (HD), which occurs in approximately 1 in 5000 births.

HD occurs during the first 12 weeks of gestation when there is failed craniocaudal migration of neuroblasts originating from the neural crest. This results in functional intestinal obstruction, with most cases presenting before age 5. HD is not commonly seen in adults, as most patients are diagnosed early in life and are treated surgically. However, some patients with mild symptoms may go undiagnosed into adulthood and manage their symptoms with cathartic agents. Presumably, the colon segment proximal to the obstructed area can assume a compensatory role. However, at some point, the dilated proximal colonic segment may decompensate secondary to the distal obstruction. It has been reported that these patients can experience a rapid worsening in their constipation or even acute obstruction. Anorectal manometry would demonstrate an absence of the rectal anal inhibitory reflex. Deep rectal biopsy will establish the diagnosis of HD with the total absence of intramural ganglion cells of the submucosal (Meissner) and myenteric (Auerbach) neural plexuses in the affected colon segment. Computed tomography scan may show a dilated colon, but this does not establish the diagnosis. Barium enema has a low sensitivity for HD, but may reveal a “transition zone,” which represents the change from the normal caliber/narrowed rectum (aganglionic segment) to the dilated colon proximal to the aganglionic region. Although this finding is fairly specific for HD, it is not sufficient to make the diagnosis. Colonoscopy cannot make a diagnosis of HD.

REFERENCE

Qiu JF, Shi YJ, Hu L, Fang L, Wang HF, Zhang MC. Adult Hirschsprung's disease: report of four cases. *Int J Clin Exp Pathol*. 2013;6(8):1624-1630. Published 2013 Jul 15.

Question 6

A 40-year-old man presents to his primary care provider with a change in his bowel movements. He reports a decreased frequency, having a bowel movement only every 2 to 3 days. He also thinks he may not have been eating as much and has lost

a little weight. He does feel a little uncomfortable in his abdomen. Occasionally, he notes blood in his bowel movement. What test will establish the diagnosis?

- A. Complete blood count
- B. Pudendal nerve terminal latency test
- C. Anorectal manometry
- D. Colonoscopy

CORRECT ANSWER: D

RATIONALE

Colorectal cancer can be a cause for change in bowel habits, causing constipation/obstipation. The patient's complaints combined with weight loss and rectal bleeding is concerning. With the rise in incidence of early-onset colorectal cancer, the diagnostic test of choice would be colonoscopy. Although a complete blood count may show anemia, this would not establish a diagnosis. Pudendal nerve terminal latency test is used in the evaluation of fecal incontinence. Anorectal manometry can evaluate for defecatory disorders; however, in a patient with red flags such as weight loss and rectal bleeding, a colonoscopy is warranted first.

REFERENCE

Astin M, Griffin T, Neal RD, Rose P, Hamilton W. The diagnostic value of symptoms for colorectal cancer in primary care: a systematic review. *Br J Gen Pract.* 2011;61(586):e231-e243. doi:10.3399/bjgp11X572427

Question 7

A 36-year-old woman with a history of constipation reports that it has worsened since her last pregnancy 2 years ago. Despite the use of polyethylene glycol twice daily, she complains of straining and small, infrequent bowel movements. She never feels fully evacuated. She has to push on her perineum to help evacuate the stool.

What is the next best step?

- A. Anorectal manometry
- B. Colonoscopy
- C. Defecography
- D. Digital rectal exam
- E. Referral to colorectal surgery

CORRECT ANSWER: D

RATIONALE

This patient is presenting with complaints consistent with dyssynergic defecation, including straining, incomplete evacuation with small stools, and use of manual maneuvers to improve defecation. Risk factors include history of painful defecation or withholding of stool, anorectal trauma, back injury, or sexual abuse. The role of pregnancy and obstetrical complications is controversial; in some studies, it has been shown to be a risk factor, but not in others. The first step in evaluating for a defecatory disorder is a digital rectal examination (DRE), which can help exclude other causes of obstructed defecation, such as an anal or rectal mass, rectocele, or rectal prolapse. Findings on DRE that are suggestive of dyssynergic defecation include contraction of the diaphragm, abdomen, and rectum during push maneuvers (abdominal pressure and rectal examination must be performed simultaneously) and abnormal relaxation of external anal sphincter and puborectalis muscles (or no relaxation with Valsalva maneuver). The sensitivity and specificity of DRE for identifying dyssynergia in patients with chronic constipation is 75% and 87%, respectively; the positive predictive value is 97%. DREs can facilitate the selection of appropriate patients for further physiologic testing with anorectal manometry.

Colonoscopy is not warranted in this young patient with chronic symptoms and no alarm features. Defecography and anorectal manometry are both useful in evaluating a defecatory disorder but should always be done after a DRE. Referral to colorectal surgery may be needed if a structural problem is found but would not be the next step here.

REFERENCES

Lacy BE, Pimentel M, Brenner DM, et al. ACG

Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036

Rao SS, Patcharatrakul T. Diagnosis and Treatment of Dyssynergic Defecation. *J Neurogastroenterol Motil*. 2016;22(3):423-435. doi:10.5056/jnm16060

Tantiphlachiva K, Rao P, Attaluri A, Rao SS. Digital rectal examination is a useful tool for identifying patients with dyssynergia. *Clin Gastroenterol Hepatol*. 2010;8(11):955-960. doi:10.1016/j.cgh.2010.06.031

Question 8

A 64-year-old man with a history of hyperlipidemia, hypertension, and diabetes mellitus is seeing his primary care provider for a health maintenance examination.

On review, he reports intermittent hard stools. In reviewing his medication list, which medicine is most often associated with constipation?

- A. Lovastatin
- B. Insulin
- C. Metformin
- D. Amlodipine

CORRECT ANSWER: D

RATIONALE

Whenever a patient presents with new-onset constipation, the medication list should be scrutinized for potential causes. The most common pharmacologic causes of constipation include opiates, anticholinergic agents (eg, tricyclic antidepressants, antiparkinsonian drugs), calcium channel blockers, and anticonvulsants. Of the listed medications, amlodipine is the most likely culprit. Statins are sometimes associated with microscopic colitis and diarrhea. Insulin is not known to cause bowel changes. Metformin is associated with diarrhea in up to 30% of patients.

REFERENCE

Lembo A, Ullman SP. Constipation. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*, 10th ed. Elsevier, Inc; 2016:259-284.

Question 9

A 65-year-old man with a history of Parkinson disease (PD) presents to a gastroenterologist with gastrointestinal symptoms.

What is the most likely gastrointestinal manifestation prompting his presentation?

- A. Malnutrition
- B. Dysphagia
- C. Delayed gastric emptying
- D. Constipation

CORRECT ANSWER: D

RATIONALE

Patients with PD may present with a myriad of gastrointestinal (GI) symptoms. The GI system manifestations occur in the early stages of the disease, in some cases even before the occurrence of the motor symptoms. Dysphagia occurs in 9% to 82% of patients with PD. Malnutrition occurs in up to 24% of patients. Delayed gastric emptying is common but not always manifested. Constipation is the most common GI manifestation of PD and is reported in 80% to 90% of cases. The medications used for PD are also common causes of constipation due to their anticholinergic effects.

REFERENCE

Ivan IF, Irincu VL, Diaconu Ș, Falup-Pecurariu O, Ciopleiaș B, Falup-Pecurariu C. Gastro-intestinal dysfunctions in Parkinson's disease (Review). *Exp Ther Med*. 2021;22(4):1083. doi:10.3892/etm.2021.10517

Question 10

A 30-year-old woman is being seen by her pri-

mary care provider for her health maintenance examination. She reports infrequent hard stools approximately 2 times weekly. She denies any blood in her stool. Her hemoglobin is 13.1 mg/dL (reference range [female], 12-16 mg/dL).

What is the next best step in management of this patient?

- A. Docusate
- B. Senna
- C. Lubiprostone
- D. Psyllium

CORRECT ANSWER: D

RATIONALE

The use of psyllium is indicated as first-line treatment in people with chronic intermittent constipation without alarm features. Lubiprostone should be used for those who do not respond to more conservative measures of fiber supplementation and osmotic laxatives. Docusate is an emollient that may coat the stool and help with straining but will not help with infrequent defecation as this patient has. Senna can be used in this situation but has side effects of cramping and, thus, could be considered if fiber supplementation does not work.

REFERENCE

Bharucha AE, Dorn SD, Lembo A, Pressman A. American Gastroenterological Association medical position statement on constipation. *Gastroenterology*. 2013;144(1):211-217. doi:10.1053/j.gastro.2012.10.029

Question 11

A 68-year-old woman with hypertension and longstanding irritable bowel syndrome with constipation (IBS-C) comes to you for a second opinion. She has had a normal anorectal manometry and magnetic resonance defecography. She is being treated with polyethylene glycol twice daily, with incomplete relief. She has tried senna in the past, but this caused severe cramping. She complains of

bowel movements every other day with straining and bloating and abdominal discomfort relieved with defecation.

What is the next best step?

- A. Add docusate twice daily
- B. Add psyllium
- C. Increase polyethylene glycol to three times daily
- D. Stop polyethylene glycol and start linaclotide
- E. Stop polyethylene glycol and start tegaserod

CORRECT ANSWER: D

RATIONALE

Linaclotide is a guanylate cyclase C agonist that acts as a chloride secretagogue to pull water into the intestinal lumen, increasing peristalsis. Preclinical trials identified reduced activation of visceral nociceptive neurons with the use of linaclotide. This can lead to improvement in constipation and global IBS symptoms in patients with IBS-C. Guidelines recommend the use of linaclotide for IBS-C.

Adding a stool softener such as docusate will not help in patients who do not respond to polyethylene glycol. There is no evidence that polyethylene glycol alleviates abdominal pain and, thus, global symptoms in patients with IBS-C and the American College of Gastroenterology guidelines on treatment of IBS recommend against its use alone for the treatment of global IBS-C symptoms. Tegaserod is the only 5-HT₄ receptor agonist approved by the US Food and Drug Administration for the treatment of women with IBS-C. It is contraindicated in patients greater than 65 years of age or with more than 1 cardiovascular risk factor, due to an increased risk of major cardiovascular events in this population.

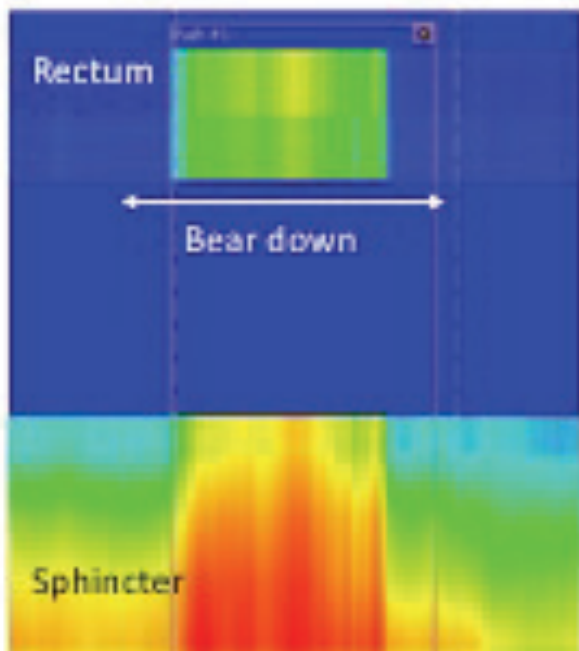
REFERENCES

Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036

Rao S, Lembo AJ, Shiff SJ, et al. A 12-week, randomized, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. *Am J Gastroenterol*. 2012;107(11):1714-p.1725. doi:10.1038/ajg.2012.255

Question 12

A 37-year-old woman with history of constipation is seen by her gastroenterologist. She has not noted a change in her symptoms with psyllium. She complains of hard stools with significant straining and reports the need to use manual maneuvers to evacuate her bowels. High-resolution anorectal manometry demonstrates the following:



What is the best next step in management of this patient?

- A. Polyethylene glycol
- B. Docusate
- C. Biofeedback therapy
- D. Abdominal colonic massage

CORRECT ANSWER: C

RATIONALE

This high-resolution anorectal manometry demonstrates a type 1 pattern of dyssynergic defecation with an appropriate increase in rectal pressure and an inappropriate contraction of the anal sphincter. Biofeedback is first-line treatment for patients with dyssynergic defecation, with a 70% to 80% efficacy rate.

REFERENCE

Rao SS, Benninga MA, Bharucha AE, Chiarioni G, Di Lorenzo C, Whitehead WE. ANMS-ESNM position paper and consensus guidelines on biofeedback therapy for anorectal disorders. *Neurogastroenterol Motil*. 2015;27(5):594-609. doi:10.1111/nmo.12520

Question 13

A 32-year-old woman with a 10-year history of constipation is seen in follow-up by her gastroenterologist. She has not noted a change in her symptoms with psyllium and polyethylene glycol. What is the best next step in management?

- A. Anorectal manometry
- B. Barium enema
- C. Colonoscopy
- D. Pudendal nerve terminal latency test

CORRECT ANSWER: A

RATIONALE

Patients who have failed initial therapy may benefit from additional evaluation with physiological tests of outlet function such as anorectal manometry or defecography. If an abnormality is discovered, therapy directed at the abnormal physiology may prove helpful.

REFERENCE

Bharucha AE, Dorn SD, Lembo A, Pressman A. American Gastroenterological Association medical position statement on constipation. *Gastroenterology*. 2013;144(1):211-217. doi:10.1053/j.gastro.2012.10.029

Question 14

A 65-year-old man with a history of chronic back presents with complaints of constipation. He is taking morphine daily to control his pain. He has noted hard, infrequent stools, less than twice weekly. He reports living with this for a long time and now wants help.

What is the best medication to order?

- A. Methylnaltrexone
- B. Naldemedine
- C. Polyethylene glycol
- D. Alvimopan

CORRECT ANSWER: C

RATIONALE

It is suggested to start with conventional laxatives as first-line agents in opioid-induced constipation. The choice of agent and the dosing are empiric. This first-line would include osmotic laxatives (PEG, lactulose, magnesium citrate, magnesium hydroxide), stimulant laxatives (bisacodyl, sodium picosulfate, senna), detergent/surfactant stool softener (docusate), and lubricant stool softener (mineral oil). For patients who fail conventional laxatives, the next step would be to try peripherally active mu-opioid receptor antagonists such as methylnaltrexone, naldemedine, and alvimopan.

REFERENCE

Crockett SD, Greer KB, Heidelbaugh JJ, et al. American Gastroenterological Association Institute Guideline on the Medical Management of Opioid-Induced Constipation. *Gastroenterology*. 2019;156(1):218-226. doi:10.1053/j.gastro.2018.07.016

Question 15

Which of the following is the mechanism of action of linaclotide?

- A. It exerts its effect via activation of type 2 chloride channels (CLC-2) on the apical

membrane of epithelial cells, which leads to higher chloride concentrations in the intestinal fluid, which increases water secretion in the intestinal lumen, ultimately causing accelerated intestinal and colonic transit

- B. It is an inhibitor of the gastrointestinal sodium/hydrogen exchanger isoform 3 (NHE3), which increases the excretion of sodium and fluid in stool
- C. It binds to and activates the guanylate cyclase type C receptors, which leads to an increase in intracellular cyclic guanosine monophosphate (cGMP) and stimulates chloride secretion through the cystic fibrosis transmembrane regulator. This results in an increase in water secretion into the intestinal lumen, accelerating intestinal transit
- D. It binds to the serotonin-4 receptor and stimulates peristaltic reflex and intestinal secretion

CORRECT ANSWER: C

RATIONALE

Linaclotide works in patients with chronic intermittent constipation by binding to and activating the guanylate cyclase type C receptors, which leads to an increase in intracellular cGMP and stimulates chloride secretion through the cystic fibrosis transmembrane regulator. This results in an increase in water secretion into the intestinal lumen, accelerating intestinal transit. Lubiprostone is a bicyclic fatty acid, derived from prostaglandin E1, which exerts its effect via activation of type 2 CLC-2 on the apical membrane of epithelial cells. The CLC-2 activation leads to higher chloride concentrations in the intestinal fluid, which increases water secretion in the intestinal lumen, ultimately causing accelerated intestinal and colonic transit. Tenapanor is a small-molecule inhibitor of the gastrointestinal NHE3. This NHE3 inhibition increases the excretion of sodium and fluid in stool. This medication is used for IBS-C and is not available in the United States. Finally, tegaserod is not a secretagogue, it is a prokinetic that binds to the serotonin-4 receptor and stimulates peristaltic reflex and intestinal secretion.

REFERENCE

Bharucha AE, Dorn SD, Lembo A, Pressman A. American Gastroenterological Association medical position statement on constipation. *Gastroenterology*. 2013;144(1):211-217. doi:10.1053/j.gastro.2012.10.029

Question 16

A 52-year-old man with cerebral palsy and chronic constipation presents to the emergency department with worsening abdominal distension, nausea, and vomiting. Radiography is performed, which reveals a large loop of distended colon with its long axis extending from the right lower quadrant to the left upper quadrant. There are a few air fluid levels in this area, but the rest of the bowel is normal appearing.

What is the next best step?

- A. Flexible sigmoidoscopy
- B. Nasogastric tube to low intermittent wall suction
- C. Neostigmine
- D. Rectal tube and tap water enemas
- E. Segmental colectomy

CORRECT ANSWER: A

RATIONALE

This is a classic case of a sigmoid volvulus. Volvulus occurs from a torsion of a redundant segment of colon. These most commonly occur in the sigmoid colon. Risk factors include constipation, prior abdominal surgery, colonic dysmotility, immobility, and redundant colon with a narrow mesenteric attachment. Sigmoid volvulus is treated with endoscopic reduction by passing the endoscope beyond the point of obstruction by gently passing the scope through the twisted segment. If this is successful, aggressive suctioning of the colon segment should be performed. In addition to being a therapeutic modality, endoscopy allows for assessment of colon viability. Successful endoscopic treatment of sigmoid

volvulus occurs in 55% to 94% of patients, although recurrence is up to 87%. Nasogastric tube or rectal tube and enemas can be used for colonic pseudo-obstruction but will not detorse a volvulus. Neostigmine should not be used in the setting of a volvulus. Segmental colectomy is likely needed, but acute endoscopic decompression should be done first to decrease the morbidity of the operation.

REFERENCE

Naveed M, Jamil LH, Fujii-Lau LL, et al. American Society for Gastrointestinal Endoscopy guideline on the role of endoscopy in the management of acute colonic pseudo-obstruction and colonic volvulus. *Gastrointest Endosc*. 2020;91(2):228-235. doi:10.1016/j.gie.2019.09.007

Question 17

All the following are metabolic disturbances that can lead to secondary constipation except:

- A. Hypercalcemia
- B. Hypophosphatemia
- C. Hypomagnesemia
- D. Hypokalemia

CORRECT ANSWER: B

RATIONALE

It is important to understand secondary causes of constipation. Metabolic disorders are a common cause of constipation. Thus, screening with a thyroid-stimulating hormone and comprehensive metabolic panel is reasonable. Hypothyroidism, hypercalcemia, hypomagnesemia, and hypokalemia all can lead to secondary constipation. Low phosphate is not associated with constipation.

REFERENCE

Lembo A, Ullman SP. Constipation. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*, 10th ed. Elsevier, Inc; 2016:259-284.

Question 18

A 52-year-old man with history of diabetes mellitus for 10 years is being seen by his gastroenterologist. For the past 3 to 5 years, he reports having 1 to 2 bowel movements weekly with a type 1 stool on the Bristol Stool Scale. He recently had a colonoscopy for colon cancer screening, which was normal. The mechanisms causing his complaint include all the following except:

- A. A reduction in density of interstitial cells of Cajal in the colon
- B. Myopathic changes resulting in colonic wall thickening, decreased compliance, and a reduction in the relaxation as well as muscle contraction
- C. The neuronal degeneration and neuronal reduction of the myenteric plexus of the colon
- D. The upregulation of serotonergic 5-hydroxytryptamine receptors and an excess release of serotonin

CORRECT ANSWER: D

RATIONALE

The underlying mechanisms for constipation associated with diabetes mellitus is multifactorial. Known and emerging mechanisms include neuropathic injury and alteration to the autonomic nervous system, enteric nervous system, and interstitial cells of Cajal, as well as direct myopathic changes to the smooth muscle. The neuropathic effects of diabetes can involve the entire gastrointestinal tract including the colon. There are well-described changes in the vagus nerve that include axonal degeneration, segmental demyelination, and a reduction in motor as well as sensory ganglions, which are also presumed to involve the autonomic nerves of the colon. Emerging evidence has demonstrated myopathic changes from an increase in the production of collagen are thought to be a result of increased glycation end-products. This leads to a remodeling of the muscle layer of the colon resulting in colonic wall thickening, decreased compliance, and a reduction in the relaxation

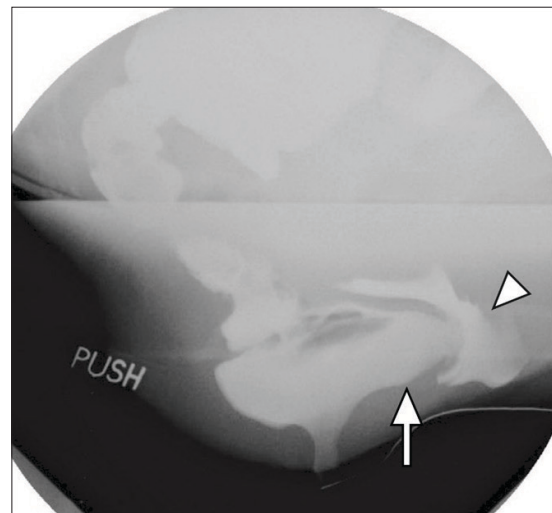
as well as muscle contraction. Both the diabetes mellitus-induced neuropathic and myopathic effects on the colon lead to altered colonic motility, modification of the colonic microbiota, and altered sensory as well as motor responses of the colon.

REFERENCE

Piper MS, Saad RJ. Diabetes Mellitus and the Colon. *Curr Treat Options Gastroenterol*. 2017;15(4):460-474. doi:10.1007/s11938-017-0151-1

Question 19

A 53-year-old woman with a history of hypertension, diabetes mellitus, and irritable bowel syndrome-constipation (IBS-C) is being seen by a gastroenterologist. She complains of incomplete evacuation, bloating, and having to push vaginally to empty her rectum. Below is a diagnostic study ordered by the doctor.



What is the next step in the care of this patient?

- A. Urogynecology referral
- B. Polyethylene glycol
- C. Increase hydration
- D. Anorectal manometry

CORRECT ANSWER: D

RATIONALE

Rectocele is a type of pelvic organ prolapse that is a herniation of the rectum into the posterior vaginal wall that results in a vaginal bulge. Some women may be asymptomatic, whereas others may experience a significant impact on their quality of life, including the following symptoms: constipation, obstructive defecation, incomplete defecation, pelvic pain/pressure, posterior vaginal bulge, dyspareunia and vaginal erosions, and mucosal bleeding. Symptoms do not predict anatomic findings and anatomic findings do not reliably predict symptoms associated with posterior vaginal prolapse. Determining whether the observed anatomy is the result or cause of the problem is challenging; thus, it is important to evaluate for dyssynergia, and if present, treat with biofeedback before any rectocele surgery. Treating constipation with increased hydration and/or osmotic laxatives will not address the complaints of obstructed defecation and therefore are not the best options here.

REFERENCES

- Hale DS, Fenner D. Consistently inconsistent, the posterior vaginal wall. *Am J Obstet Gynecol*. 2016;214(3):314-320. doi:10.1016/j.ajog.2015.09.001
- Iglesia CB, Smithling KR. Pelvic Organ Prolapse. *Am Fam Physician*. 2017;96(3):179-185.

Question 20

A 53-year-old woman with a history of hypertension, hyperlipidemia, and obesity is being seen by a gastroenterologist for constipation. She complains of straining and incomplete emptying. She has a bowel movement every 2 days. She has tried fiber products and polyethylene glycol without relief. Digital rectal examination, colonoscopy, and anorectal manometry are normal. What should you do next?

- A. Start tegaserod
- B. Scrutinize her medication list

- C. Refer to colorectal surgery
- D. Start linaclotide

CORRECT ANSWER: B

RATIONALE

It is important to recognize secondary causes of constipation, which commonly include medications. Calcium channel blockers, anticonvulsants, antiparkinsonian drugs, opiates, and psychotropic medications are common causes. This patient has hypertension and is likely on a calcium channel blocker. Tegaserod is a 5-hydroxytryptamine(4) agonist that can be used for irritable bowel syndrome with constipation but is contraindicated in patients with more than 1 cardiovascular risk factor, so it would not be used in this patient. Referring to colorectal surgery at this point would be premature, as the patient has not tried any prescription medications for her constipation. Linaclotide would be an appropriate next step; however, her medication list should be reviewed first to identify medications that could be worsening her symptoms.

REFERENCE

- Bharucha AE, Dorn SD, Lembo A, Pressman A. American Gastroenterological Association medical position statement on constipation. *Gastroenterology*. 2013;144(1):211-217. doi:10.1053/j.gastro.2012.10.029

Question 21

A 30-year-old woman with a history of constipation is being seen by her gastroenterologist. She reports going to the emergency department for acute loss of vision in her left eye. She was diagnosed with optic neuritis and treated with steroids. What is the likely disease that is associated with her constipation?

- A. Myelomeningocele
- B. Parkinson disease
- C. Multiple sclerosis
- D. Amyotrophic lateral sclerosis

CORRECT ANSWER: C

RATIONALE

This is a presentation of a young woman with multiple sclerosis (MS). Constipation is present in almost half of patients with MS and can precede the diagnosis of MS by many years. The precise neuropathological mechanism for constipation in MS is not defined; however, the disease process can affect multiple neurologic pathways directly and at multiple levels.

REFERENCES

Awad RA. Neurogenic bowel dysfunction in patients with spinal cord injury, myelomeningocele, multiple sclerosis and Parkinson's disease. *World J Gastroenterol*. 2011;17(46):5035-5048. doi:10.3748/wjg.v17.i46.5035

Preziosi G, Gordon-Dixon A, Emmanuel A. Neurogenic bowel dysfunction in patients with multiple sclerosis: prevalence, impact, and management strategies. *Degener Neurol Neuromuscul Dis*. 2018;8:79-90. Published 2018 Dec 6. doi:10.2147/DNND.S138835

Question 22

A 41-year-old woman with a long history of constipation and a bowel movement every 10 days is being seen by a gastroenterologist. She has tried fiber, polyethylene glycol 3350, sorbitol, senna, bisacodyl, lubiprostone, linaclotide, and prucalopride without meaningful success. She is tired of not having a bowel movement and wants to be referred for surgery. Which of the following would be a contraindication to subtotal colectomy if found?

- A. Normal transit on wireless motility capsule
- B. Dyssynergic defecation on anorectal manometry
- C. Rectocele on defecography
- D. Abnormal pudendal nerve terminal motor latency test

CORRECT ANSWER: A

RATIONALE

Surgical approaches to constipation should be reserved for patients who have failed medical management. Patients should have a complete evaluation with physiologic tests to exclude functional outlet obstruction because subtotal colectomy with ileorectal anastomosis is only considered for severe and intractable slow transit constipation. If the patient has normal transit, they are not a candidate for surgery. Dyssynergic defecation would require treatment and evidence of normal functioning before surgery. An abnormal pudendal nerve would not impact the decision for surgery, and it is not a test that is commonly ordered.

REFERENCES

Wilkinson-Smith V, Bharucha AE, Emmanuel A, Knowles C, Yiannakou Y, Corsetti M. When all seems lost: management of refractory constipation—Surgery, rectal irrigation, percutaneous endoscopic colostomy, and more. *Neurogastroenterol Motil*. 2018;30(5):e13352. doi:10.1111/nmo.13352

Question 23

A 45-year-old woman with a history of hyperlipidemia and refractory constipation is being seen by a colorectal surgeon for consideration of a subtotal colectomy with ileorectal anastomosis. Which of the following long-term surgical outcomes are correct?

- A. Almost 20% of patients have persistent constipation after a colectomy
- B. 30% to 35% of patients report diarrhea and fecal incontinence
- C. 20% to 25% of patients report abdominal pain
- D. 50% of patients complain of bloating

CORRECT ANSWER: A

RATIONALE

The following are typical long-term surgical out-

comes following surgery for slow transit constipation: 18.2 % of patients had persistent constipation after a colectomy; 5% to 15% of patients had diarrhea and fecal incontinence; 30% to 50% of patients had abdominal pain; and 10% to 40% of patients had bloating.

REFERENCE

Knowles CH, Grossi U, Chapman M, Mason J; NIHR CapaCiTY working group; Pelvic floor Society. Surgery for constipation: systematic review and practice recommendations: Results I: Colonic resection. *Colorectal Dis.* 2017;19 Suppl 3:17-36. doi:10.1111/codi.13779

Question 24

A 74-year-old man with a history of coronary heart disease after coronary artery bypass grafting x 3 vessels and recent acute atrial fibrillation is now complaining of 3 days without a bowel movement, general abdominal pain, and progressive distension of his abdomen. Physical examination demonstrates no bowel sounds, distended abdomen without rebound or guarding.

His abdominal radiograph shows the following:



IMAGE COURTESY OF THE RADSWIKI, RADIOPAEDIA.ORG, RID: 11684

What is first step in management?

- A. Colonoscopy
- B. Barium enema
- C. Nasogastric tube
- D. Intravenous pyridostigmine

CORRECT ANSWER: C

RATIONALE

Acute colonic pseudo-obstruction (Ogilvie syndrome) is a presentation of acute constipation/abdominal pain associated with massive dilation of the colon in the absence of mechanical etiology of obstruction. Most patients with this disorder are hospitalized. The exact mechanism is unknown; however, multiple risk factors have been elucidated including critical illness, nonoperative trauma, surgical procedures, and metabolic imbalance. The first steps when there is no evidence for ischemia or perforation: restricting oral intake, using nasogastric and/or rectal tube to intermittent suction, stopping offending agents, and correcting fluid and electrolytes. Risk of perforation increases in those with distention of greater than 6 days and with cecal diameters 12 cm or more. If the patient has partial or no response after 48 hours to 72 hours, either pharmacologic management with neostigmine or endoscopic decompression is recommended. If the patient fails these measures, then surgical intervention is required. However, mortality rates are high (up to 44%) in patients undergoing surgery, so all should be done to manage this disorder nonoperatively.

REFERENCE

Naveed M, Jamil LH, Fujii-Lau LL, et al. American Society for Gastrointestinal Endoscopy guideline on the role of endoscopy in the management of acute colonic pseudo-obstruction and colonic volvulus. *Gastrointest Endosc.* 2020;91(2):228-235. doi:10.1016/j.gie.2019.09.007

Question 25

79-year-old man with a history of paraplegia is

sent to the emergency department from the nursing home for increasing nausea, abdominal pain, abdominal distension, and constipation. In the emergency department, vital signs are as follows: blood pressure, 116/88 mmHg; heart rate, 95 bpm; oxygen saturation, 97%. Physical examination is significant for a distended abdomen with absent bowel sounds, without rebound or guarding.

Abdominal radiography demonstrated the following:

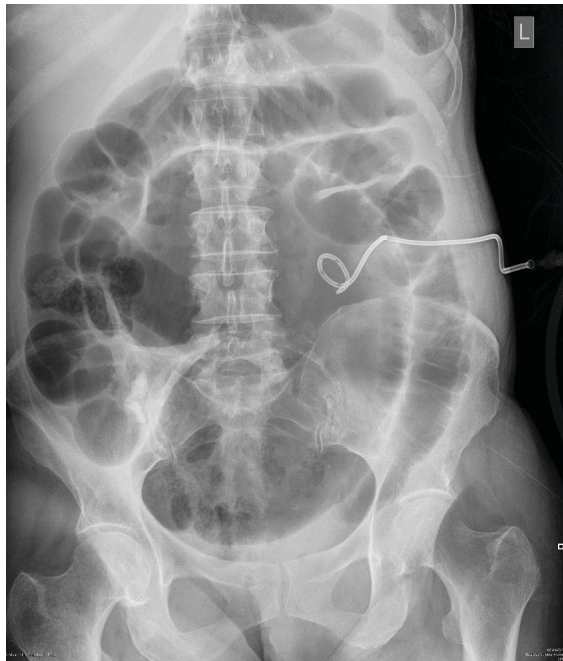


IMAGE COURTESY OF DR IAN BICKLE, RADIOPAEDIA.ORG, RID: 33334

What is the next step in management?

- A. Contrast-enhanced computed tomography
- B. Right hemicolectomy
- C. Colonoscopy
- D. Intravenous neostigmine

CORRECT ANSWER: B

RATIONALE

This radiograph represents cecal volvulus, with the classic finding of marked distension of a loop of large bowel with its long axis extending from the right lower quadrant to the epigastrium or left

upper quadrant. Volvulus occurs from a torsion of a redundant segment of colon. These commonly occur in the cecum or sigmoid colon. Risk factors include constipation, prior abdominal surgery, colonic dysmotility, and redundant colon with a narrow mesenteric attachment. Cecal and sigmoid volvulus are managed differently. Cecal volvulus is treated with surgical management as endoscopic reduction is rarely effective and there is an increased risk of perforation. Sigmoid volvulus is treated with endoscopic reduction by passing the endoscope beyond the point of obstruction by gently passing the scope through the twisted segment. If this is successful, aggressive decompression of the colon segment should be performed. Successful endoscopic treatment of sigmoid volvulus occurs in 55% to 94% of patients, although recurrence is up to 87%.

REFERENCE

Naveed M, Jamil LH, Fujii-Lau LL, et al. American Society for Gastrointestinal Endoscopy guideline on the role of endoscopy in the management of acute colonic pseudo-obstruction and colonic volvulus. *Gastrointest Endosc.* 2020;91(2):228-235. doi:10.1016/j.gie.2019.09.007

Question 26

A 24-year-old healthy woman presents to the office for evaluation of chronic intermittent diarrhea and abdominal pain. She reports 6 years of watery, nonbloody diarrhea (Bristol Stool Scale, 6) from 2 to 5 times daily with associated lower abdominal cramping discomfort that is moderately improved with bowel movements. There is no clear symptom association with food; however, she notices symptoms worsen with increased stress at work and home. She denies blood in the stool, weight loss, fecal incontinence, and nocturnal bowel movements. She does not take any medications, has no recent antibiotic exposure, and has no surgical or travel history. Her family history is relevant for a sister with Crohn's disease and brother with autoimmune hypothyroid disease. There is no family history of colorectal cancer. Her physical exami-

nation is unremarkable. Initial blood work shows normal complete blood count and comprehensive metabolic panel.

Which of the following additional testing is most appropriate at this time?

- A. Stool studies for *Clostridium difficile*, culture, and ova and parasites
- B. Colonoscopy with random colon biopsies
- C. Glucose hydrogen breath test
- D. Fecal calprotectin and anti-tissue transglutaminase IgA
- E. Fecal pancreatic elastase

CORRECT ANSWER: D

RATIONALE

This patient's symptoms are most suggestive of irritable bowel syndrome-diarrhea predominant (IBS-D), based upon Rome IV criteria (recurrent abdominal pain associated with defecation and change in stool frequency and form). She has no concerning alarm signs or symptoms and no high-risk history to suggest alternative concerning pathology. Current guidelines suggest performing limited diagnostic testing in the setting of suspected IBS-D to rule out common alternative diagnoses and tailor further evaluation based predominantly upon risk factors and signs/symptoms. A positive diagnostic strategy as compared with a diagnostic strategy of exclusion for patients with symptoms of IBS is favored to improve cost-effectiveness and reduce unnecessary testing. The most appropriate additional testing in this patient's clinical scenario is to rule out celiac disease, another common treatable cause of chronic diarrhea, with an anti-tissue transglutaminase IgA with total IgA levels. In addition, she should be evaluated for inflammatory diarrhea with fecal calprotectin (or fecal lactoferrin) and possibly C-reactive protein. A negative fecal calprotectin and C-reactive protein have a very high negative predictive value for inflammatory bowel disease. Additional testing beyond this is unnecessary in this clinical scenario.

This patient does not have any travel or other risk factors for infectious diarrhea, and routine stool testing for enteric pathogens is not recommended in patients with IBS (answer A). She also lacks alarm symptoms as well as risk factors (taking medications such as nonsteroidal anti-inflammatory drugs, smoking) or the typical clinical profile (middle-aged female with frequent diarrhea) for microscopic colitis; therefore, a colonoscopy with biopsy is not the best next step (answer B). Although the differential diagnosis for her symptoms could also include small intestinal bacterial overgrowth (answer C) and exocrine pancreatic insufficiency (answer E), she lacks typical risk factors for these conditions, and these are not currently recommended initial diagnostic tests for IBS-D. However, should she fail to respond to typical IBS-D treatments, additional testing with some of the other answer choices can be considered to rule out alternative diagnoses.

REFERENCES

- Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036
- Smalley W, Falck-Ytter C, Carrasco-Labra A, Wani S, Lytvyn L, Falck-Ytter Y. AGA Clinical Practice Guidelines on the Laboratory Evaluation of Functional Diarrhea and Diarrhea-Predominant Irritable Bowel Syndrome in Adults (IBS-D). *Gastroenterology*. 2019;157(3):851-854. doi:10.1053/j.gastro.2019.07.004

Question 27

A 19-year-old man presents to the office with 6 weeks of diarrhea. He reports being in his usual state of health until 6 weeks ago when he was camping and swimming in the mountains with his family. Upon returning from camping, he notices abdominal bloating, increased gas, lower abdominal cramping, and loose nonwatery diarrhea 4 to 8 times daily (Bristol Stool Scale, 7). He believes that his stool appears to be floating and oily ap-

pearing. He takes no medications and has no past medical or surgical history. Physical examination is unremarkable.

Which of the following will most likely assist in diagnosing the cause of this patient’s diarrhea?

- A. Stool for *Clostridium difficile* toxin A and B enzyme immunoassay
- B. Stool polymerase chain reaction (PCR) for *Escherichia coli*, *Shigella*, *Campylobacter*
- C. Stool PCR for Giardia
- D. Stool microscopy for ova and parasites
- E. Fecal calprotectin and anti-tissue transglutaminase IgA

CORRECT ANSWER: C

RATIONALE

Giardia lamblia infection (giardiasis) is a common protozoal pathogen in the United States. Risk factors for Giardia infection include drinking water or swimming, camping, or hiking in places where Giardia may live, such as untreated or improperly treated water from lakes, streams, or wells. In this case, the patient’s travel to a remote location and close contact with untreated water increases the likelihood that his chronic diarrhea is caused by giardiasis. Testing for giardiasis is therefore recommended in patients with chronic diarrhea, particularly in those with a history of travel to developing countries or to endemic areas and in those in contact with poor water quality, camping, and daycare exposure. Testing is with stool Giardia antigens or PCR, both have excellent performance characteristics, with sensitivity and specificity of more than 95%. Treatment is readily available and well tolerated; therefore, further emphasizing the ease and importance of ruling out chronic Giardia infection in patients with chronic diarrhea and risk factors.

The other answers are incorrect because the patient does not have risk factors for infection with *Clostridium difficile*, bacterial enteric pathogens, or ova and parasites. He also lacks clinical history to suggest inflammatory bowel disease or Celiac disease.

REFERENCES

Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036

Smalley W, Falck-Ytter C, Carrasco-Labra A, Wani S, Lytvyn L, Falck-Ytter Y. AGA Clinical Practice Guidelines on the Laboratory Evaluation of Functional Diarrhea and Diarrhea-Predominant Irritable Bowel Syndrome in Adults (IBS-D). *Gastroenterology*. 2019;157(3):851-854. doi:10.1053/j.gastro.2019.07.004

Question 28

A 32-year-old woman presents to your office for evaluation of chronic diarrhea. She reports 2 years of loose, poorly formed diarrhea (Bristol Stool Scale, 6) with 3 to 5 post-prandial bowel movements daily with associated gas and bloating. She denies nocturnal bowel movements, rectal bleeding, weight loss, abdominal pain, or foreign travel. She denies use of any medications. She has had a prior workup by another gastroenterologist, including normal upper endoscopy and colonoscopy with normal duodenal and colonic histology, normal complete blood count, comprehensive metabolic panel, anti-tissue transglutaminase antibodies, thyroid-stimulating hormone, stool for infectious agents and normal computed tomography of abdomen and pelvis. On physical examination, she appears anxious, but examination is otherwise unremarkable. Stool test results are as follows:

Laboratory Test	Result	Reference Range
Stool osmolality, mOsm/kg	290	<200
Stool sodium, mmol/L	42	45-150
Stool potassium, mmol/L	38	30-60

Which of the following additional tests would most likely lead to the correct diagnosis in this patient?

- A. Lactose hydrogen breath test
- B. Fecal pancreatic elastase
- C. Fecal calprotectin
- D. Scintigraphic evaluation with selenium homocholic acid taurine (SeHCAT) test
- E. Serum chromogranin A level

CORRECT ANSWER: A

RATIONALE

This patient presents with postprandial diarrhea without alarm signs or symptoms. Her prior evaluation is negative for a pathologic etiology for her diarrhea. Although the remaining differential diagnosis is broad, given the post-prandial symptoms, high consideration is made for dietary-driven symptoms such as a disaccharide intolerance and carbohydrate malabsorption. Her stool osmotic gap is elevated over 100 mosm/kg ($290 - 2(42 + 38) = 130$), supporting an osmotic diarrhea from an osmotically active stool substance such as a malabsorbed carbohydrate. The only answer choice that would lead to a diagnosis confirming osmotic diarrhea is answer A. The other answer choices are all causes of secretory diarrhea and are therefore incorrect.

The stool osmotic gap is a useful test to distinguish osmotic from secretory causes of diarrhea and is calculated with the equation $\text{Stool Osm} - 2(\text{stool Na} + \text{stool K})$, where generally 290 is assumed the value of the stool osmolality. Osmotic diarrhea has a stool osmotic gap of greater than 100 mosm/kg with increased specificity over 125 to 160 mosm/kg (due to nonelectrolytes causing an osmotic gap) whereas secretory diarrhea has a stool osmotic gap of less than 50 mosm/kg (due to retained and incomplete absorption of electrolytes such as sodium, potassium, and anions). Mixed osmotic and secretory diarrhea can be seen with an osmolar gap of 50 to 125 mosm/kg.

REFERENCE

Corinaldesi R, Stanghellini V, Barbara G, Tomassetti P, De Giorgio R. Clinical approach to diarrhea. *Intern Emerg Med*. 2012;7 Suppl 3:S255-S262. doi:10.1007/s11739-012-0827-4

Eherer AJ, Fordtran JS. Fecal osmotic gap and pH in experimental diarrhea of various causes. *Gastroenterology*. 1992;103(2):545-551. doi:10.1016/0016-5085(92)90845-p

Question 29

A 65-year-old man presents to the office for evaluation of chronic diarrhea for 2 years, abdominal bloating, and gas. He reports post-prandial diarrhea whereby approximately 15 to 20 minutes after eating his meals, he develops mild abdominal cramping, distension, and gas with associated explosive loose stool (Bristol Stool Scale, 6). He reports the symptoms are particularly worse after drinking his morning coffee with milk and eating ice cream before bed. He denies rectal bleeding, weight loss, nocturnal stools, or recent travel or antibiotic exposure. His last screening colonoscopy at age 60 was normal. Physical examination is normal.

Which of the following laboratory patterns would support this patient's diagnosis?

- A. Stool osmotic gap of 32 mosm/kg and pH of 7.2
- B. Stool osmotic gap of 44 mosm/kg and pH of 4.8
- C. Stool osmotic gap of 110 mosm/kg and pH of 6.8
- D. Stool osmotic gap of 126 mosm/kg and pH of 5
- E. Stool osmotic gap of 64 mosm/kg and pH of 7.2

CORRECT ANSWER: D

RATIONALE

This patient's clinical history of post-prandial gas, bloating, diarrhea, particularly after dairy consumption, and lack of alarm signs or symptoms are most suggestive of lactose intolerance. Diarrhea caused by carbohydrate malabsorption such as lactose can be classified as an osmotic diarrhea

with the expected stool osmotic gap being more than 100, though it is often more than 125 to 160. In addition, the fecal fluid pH is nearly always lower than 6 and usually lower than 5.3. When undigested carbohydrate reaches bacteria in the colon, bacterial fermentation of these colonic carbohydrates produces short chain fatty acids; as a result, the pH drops below 6. Diarrhea caused by other causes rarely has a pH lower than 6. Therefore, this patient’s stool profile would be expected to have an osmotic gap of more than 100 and a pH lower than 6, answer choice D.

Answers A and B would represent a secretory diarrhea (stool osmotic gap <50); answer C would represent osmotic diarrhea unrelated to carbohydrate malabsorption (pH >6); and answer E represents a possible mixed osmotic and secretory diarrhea and pH over what would be expected for carbohydrate malabsorption.

REFERENCE

Eherer AJ, Fordtran JS. Fecal osmotic gap and pH in experimental diarrhea of various causes. *Gastroenterology*. 1992;103(2):545-551. doi:10.1016/0016-5085(92)90845-p

Question 30

A 42-year-old woman presents to the office for evaluation of diarrhea. She reports 6 months of 10 to 15 watery nonbloody (Bristol Stool Scale, 7) bowel movements daily with associated abdominal cramping and some episodes of explosive diarrhea and occasional nocturnal diarrhea. She also reports occasionally flushing episodes with sudden onset of upper body and face flushing lasting from 5 to 15 minutes and an accompanying burning sensation. She has experienced a 15-pound weight loss with these symptoms. She denies association

with food, fever, or recent travel or antibiotic exposure. Physical examination reveals a right-sided cardiac murmur, no abdominal tenderness or distension, normoactive bowel sounds, and no rashes. Initial testing reveals a negative stool bacterial culture and negative *Clostridium difficile* toxins A and B with negative glutamate dehydrogenase.

Upper endoscopy and colonoscopy are normal with normal duodenal and colonic histology. A contrast enhanced triple phase computed tomography of the abdomen and pelvis reveals a soft tissue mass containing coarse central calcifications with tethered changes in the jejunum and a small 1-cm hyper enhancing liver lesion.

Stool test results are shown below.

Which of the following is the most likely pathophysiologic mechanism for the patient’s diarrhea?

- A. Poorly absorbed osmotically active substances in the colonic lumen causing luminal water retention
- B. Circulating levels of neurohormones in the blood, stimulating intestinal secretion, vasodilation, and motility, and inhibiting intestinal absorption
- C. Intestinal electrolyte malabsorption and leaky tight junction by release of cytokines
- D. Abnormal enteric nervous system causing alteration of intestinal fluid and electrolyte absorption and dysmotility
- E. Bacterial cytotoxin production leading to mucosal inflammation, cellular apoptosis, and inflammatory colonic exudate

CORRECT ANSWER: B

Laboratory Test	Result	Reference Range
Stool osmolality, mOsm/kg	290	<200
Stool sodium, mmol/L	70	45-150
Stool potassium, mmol/L	60	30-60

RATIONALE

This patient's overall clinical scenario is most consistent with carcinoid syndrome. The symptoms typical for carcinoid syndrome include diarrhea and flushing and occasionally bronchospasm, rash, and right-sided cardiac valvular abnormalities. Diagnosis is supported by suggestive clinical symptoms and confirmatory biochemical testing including 24-hour urinary excretion of 5-hydroxy-indoleacetic acid and image-based localization using cross-sectional imaging and nuclear imaging with radiolabeled somatostatin analogs such as octreotide scan or DOTATATE scan.

Diarrhea from carcinoid syndrome is thought to be secondary to effects of the neurotransmitter/neurohormone serotonin that acts to stimulate intestinal secretion, vasodilation, and motility and to inhibit intestinal absorption (answer B). The stool osmotic gap in this patient is low at 30 mosm/kg ($290 - 2(70 + 60) = 30$), and therefore supports a secretory diarrhea, which is seen with carcinoid syndrome. Secretory diarrhea has a stool osmotic gap lower than 50 mosm/kg and has a broad differential diagnosis, including many inflammatory, neoplastic, endocrine, drug-induced, dysmotility, and malabsorptive conditions.

This patient's clinical presentation and low stool osmotic gap suggests against osmotic cause of diarrhea (answer A). Cytokine effect on the bowel causing diarrhea (answer C) would be expected more with inflammatory diarrhea such as inflammatory bowel disease, which is unlikely in this patient with normal colonoscopy. Abnormal enteric nervous system effects on the bowel (answer D) would be expected with conditions such as irritable bowel syndrome or diabetic autonomic neuropathy. Bacterial cytotoxin production (an-

swer E) would be seen with *Clostridium difficile* infection, and this patient's stool was negative.

REFERENCES

- Bendelow J, Apps E, Jones LE, Poston GJ. Carcinoid syndrome. *Eur J Surg Oncol*. 2008;34(3):289-296. doi:10.1016/j.ejso.2007.07.202
- Camilleri M, Sellin JH, Barrett KE. Pathophysiology, Evaluation, and Management of Chronic Watery Diarrhea. *Gastroenterology*. 2017;152(3):515-532.e2. doi:10.1053/j.gastro.2016.10.014
- Von der Ohe MR, Camilleri M, Kvols LK, Thorforde GM. Motor dysfunction of the small bowel and colon in patients with the carcinoid syndrome and diarrhea. *N Engl J Med*. 1993;329(15):1073-1078. doi:10.1056/NEJM199310073291503

Question 31

A 28-year-old woman presents to the office with reports of chronic diarrhea. She notes several years of loose nonbloody stool (Bristol Stool Scale, 5). There is no food association, weight loss, rectal bleeding, or nocturnal stool. She has no significant past medical, family, or surgical history. Physical examination is normal. Initial blood work is notable for a normal complete blood count and thyroid stimulating hormone.

Test results are shown below.

Which of the following would explain this patient's stool laboratory profile?

- A. Carbohydrate malabsorption
- B. Stool contaminated by urine

Laboratory Test	Result	Reference Range
Stool osmolality, mOsm/kg	208	--
Stool magnesium, mmol/L	14	--
Stool potassium, mmol/L	20	--
Stool sodium, mmol/L	40	--
Plasma osmolality, mOsm/kg	288	275-295

- C. Stool sample bacterial fermentation
- D. Small intestinal bacterial overgrowth
- E. Stimulant laxative abuse

CORRECT ANSWER: B

RATIONALE

Normal fecal fluid has an expected osmolality close to that of plasma (290 mOsm/kg) because the colon itself is unable to create an osmotic gradient. A stool osmolality that varies significantly from plasma osmolality should raise concern for a contaminated or improperly collected sample. In general, a fecal osmolality greater than plasma (especially >400 mOsm/kg) suggests contamination with concentrated urine or bacterial fermentation by a specimen that was collected and left for some time. In contrast, a fecal osmolality notably less than plasma, (especially <250 mOsm/kg) suggests contamination with dilute urine or water. This patient’s stool osmolality is well below the typical expected value and therefore is most consistent with contamination from dilute urine. Such samples should not be used for calculating the stool osmotic gap nor used to determine the classification of the patient’s diarrhea.

The other answers would not be expected to result in a stool osmolality that is significantly below plasma osmolality and are incorrect.

REFERENCES

Eherer AJ, Fordtran JS. Fecal osmotic gap and pH in experimental diarrhea of various causes. *Gastroenterology*. 1992;103(2):545-551. doi:10.1016/0016-5085(92)90845-p

Shiau YF, Feldman GM, Resnick MA, Coff PM. Stool electrolyte and osmolality measurements in

the evaluation of diarrheal disorders. *Ann Intern Med*. 1985;102(6):773-775. doi:10.7326/0003-4819-102-6-773

Question 32

A 68-year-old woman presents to the office for evaluation of chronic diarrhea. She reports 6 months of watery nonbloody diarrhea (Bristol Stool Scale, 7) with 8 to 10 bowel movements daily. She has occasional episodes of waking up at night with diarrhea, but denies abdominal pain, nausea, or vomiting. The diarrhea is worse in the morning after waking up and having breakfast but continues throughout the day. She cannot make a clear association with food after keeping a food diary. She additionally denies rectal bleeding, weight loss, fatty or foul-smelling stool, or recent travel. Her medical history is notable for osteoarthritis for which she has used naproxen twice daily for years and mild gastroesophageal reflux disease for which she takes pantoprazole 20 mg daily. She smokes 1 pack daily of cigarettes for the past 30 years. Her last colonoscopy was 6 years ago and noted only sigmoid diverticulosis. She has never had an upper endoscopy. Fecal calprotectin is 64 mcg/g (normal <50 mcg/g) with a negative fecal immunochemical test. Stool for *Clostridium difficile* enzyme immunoassay, stool culture, and ova and parasites are negative.

Initial blood work is shown below.

Which of this following is the best next diagnostic test for this patient?

- A. Glucose hydrogen breath test
- B. Upper endoscopy with duodenal biopsies
- C. Fecal pancreatic elastase

Laboratory Test	Result	Reference Range
C-reactive protein, mg/dL	0.6	≤0.8
Hematocrit, blood, %	42	37-47
Hemoglobin, blood, g/dL	14	12-16
Tissue transglutaminase antibody, IgA, serum, U/mL	<0.5 (Normal total IgA)	<4.0 U/mL (Negative)

- D. Computed tomography of abdomen and pelvis with oral and intravenous contrast
- E. Colonoscopy with random colonic biopsies

CORRECT ANSWER: E

RATIONALE

This patient with chronic frequent watery diarrhea that has persisted without causative etiology despite an initial negative evaluation requires further investigation. The combination of smoking, proton pump inhibitors and nonsteroidal antiinflammatory drug (NSAID) use significantly raises the risk of microscopic colitis especially in this patient's demographic. For patients with chronic diarrhea, initial evaluation with a full history and physical examination and directed testing based upon these findings and risk factors is appropriate. If initial noninvasive testing for common causes of chronic diarrhea is negative and symptoms persist, a colonoscopy with random biopsies to evaluate for microscopic colitis is indicated, especially in the presence of risk factors for microscopic colitis (older age; female gender; frequent watery diarrhea; implicated medications such as NSAIDs, proton pump inhibitors, and selective serotonin reuptake inhibitors). This patient's fecal calprotectin is helpful to differentiate irritable bowel syndrome from inflammatory diarrhea, and although mildly elevated and nonspecific, many patients with active microscopic colitis will have minimally elevated fecal calprotectin (median, 48 µg/g) compared with those with IBS (median, 2 µg/g). This value should prompt further investigation with either repeating the test or proceeding with colonoscopy given her risk factors for microscopic colitis.

This patient lacks typical risk factors (prior abdominal surgery, dysmotility) and symptoms (bloating, gas) for small intestinal bacterial overgrowth and a colonoscopy is likely to be higher yield (answer A). Her Celiac screen with a tissue transglutaminase antibody test is negative; therefore, an endoscopy with duodenal biopsies is low yield (answer B). Similarly, she lacks typical

symptoms and risk factors for exocrine pancreatic insufficiency (answer C). A computed tomography is low yield with lack of alarm signs (weight loss, abdominal tenderness), and a colonoscopy with biopsy is a better next step before a computed tomography in this clinical scenario (answer D).

REFERENCES

Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. *Am J Gastroenterol*. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036

Masclee GM, Coloma PM, Kuipers EJ, Sturkenboom MC. Increased risk of microscopic colitis with use of proton pump inhibitors and nonsteroidal anti-inflammatory drugs. *Am J Gastroenterol*. 2015;110(5):749-759. doi:10.1038/ajg.2015.119

von Arnim U, Wex T, Ganzert C, Schulz C, Malfertheiner P. Fecal calprotectin: a marker for clinical differentiation of microscopic colitis and irritable bowel syndrome. *Clin Exp Gastroenterol*. 2016;9:97-103. Published 2016 Apr 21. doi:10.2147/CEG.S97701

Question 33

A 64-year-old woman, with history of Roux-en-Y gastric bypass and duodenal diverticulum, presents to the office for evaluation of chronic diarrhea, gas, and abdominal bloating. She has had about 2 years of mild abdominal cramping and loose stool (Bristol Stool Scale, 6), 4 to 5 times daily with associated gas and bloating with visible abdominal distension. Physical examination is notable for a body mass index of 32 kg/m² and some hyperactive bowel sounds but no tenderness, distension, or mass. Medications include oxycodone as needed for chronic back pain.

A colonoscopy with random colonic biopsies reveals normal histology and an upper endoscopy with duodenal biopsies is notable for increased intraepithelial lymphocytosis with preserved villous architecture.

Glucose hydrogen breath test and laboratory test results are shown below:

Which of the following would be the best initial treatment for this patient?

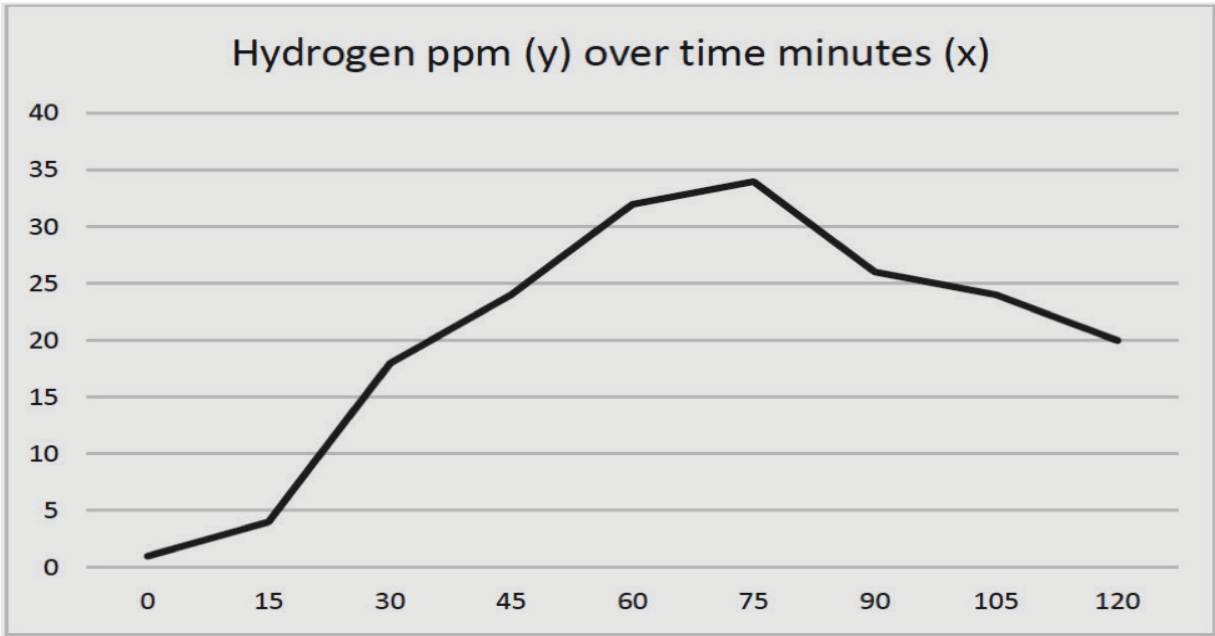
- A. Gluten-free diet
- B. Lactose-free diet
- C. Rifaximin
- D. Nortriptyline
- E. Ceftriaxone followed by trimethoprim/sulfamethoxazole

CORRECT ANSWER: C

RATIONALE

This patient’s clinical scenario is most consistent with small intestinal bacterial overgrowth (SIBO), and the most appropriate initial treat-

ment is with rifaximin. SIBO should be suspected as a cause of chronic diarrhea, bloating, gas, and abdominal distension in patients with clinical risk factors, particularly dysmotility (chronic pseudo-obstruction, diabetes with autonomic neuropathy, scleroderma, amyloidosis, opiates), prior abdominal surgery (especially bariatric surgery), anatomic abnormality (small bowel diverticulum), immunodeficiency (HIV, IgA deficiency), or malabsorptive states (chronic pancreatitis). The recommended diagnostic test is a glucose hydrogen breath test, noting an increase in hydrogen concentration of more than 20 ppm from baseline within 90 minutes, and it is preferable to small bowel aspirate due to relative ease of performance and noninvasive nature. SIBO can be associated with vitamin B12 deficiency, macrocytic anemia, and even high levels of folate due to bacterial production. Recommended treat-



Laboratory Test	Result	Reference Range
C-reactive protein, mg/dL	1.0	≤0.8
Hematocrit, blood, %	34	37-47
Hemoglobin, blood, g/dL	11.2	12-16
Mean corpuscular volume, fL	102	80-98
Tissue transglutaminase antibody, IgA, serum, U/mL	<0.5 (Normal total IgA)	<4.0 U/mL (Negative)
Vitamin B12, serum, pg/mL	80	200-800

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	12	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	14	10–40
Bilirubin, serum	0.8	0.3–1.0
Total, mg/dL	0.2	0.1–0.3
Direct, mg/dL	0.6	0.2–0.7
C-reactive protein, mg/dL	0.2	≤0.8
Fecal calprotectin, ug/g	<16	<50
Hematocrit, blood, %	42	37–47
Hemoglobin, blood, g/dL	14	12–16
Tissue transglutaminase antibody, IgA, serum, U/mL	2.1 (Normal total IgA)	<4.0 (Negative)
Total fecal bile acid (mmol/48 hours)	3246	<2337

ment is with antibiotics, with rifaximin being commonly used. Histology from the duodenum can be normal or nonspecific with increased intraepithelial lymphocytes.

This patient's presentation is not consistent with celiac disease given normal tissue transglutaminase antibody test (answer A) despite duodenal histology showing increased intraepithelial lymphocytes (which is nonspecific), nor lactose intolerance, which would not cause the observed breath test or laboratory findings (answer B). Nortriptyline is useful for treatment of abdominal pain and diarrhea in irritable bowel syndrome, which is not this patient's diagnosis (answer D). Ceftriaxone and trimethoprim/sulfamethoxazole are useful to treat Whipple's disease, of which this patient does not fit the correct demographic and does not have the typical histologic findings on endoscopy (answer E).

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Question 34

A 20-year-old woman presents to the office for evaluation of 5 years of diarrhea and abdominal pain. She reports 5 years of intermittent abdominal cramping pain associated with generally 2 to 4 loose watery nonbloody stools (Bristol Stool Scale, 6) about 4 to 5 days weekly, alternating with more formed stools (Bristol Stool Scale, 4). She notes improvement in pain with bowel movements. She has no weight loss, bleeding, nocturnal stool, or recent antibiotic exposure or travel. She does not notice any food association with her symptoms. She has no prior medical or surgical history and is not on any current medications. She denies a family history of Celiac disease or inflammatory bowel disease. Physical examination is normal.

Initial diagnostic test results are shown above.

Which of the following is the most likely pathophysiologic mechanism for this patient's diarrhea?

- Bile acid malabsorption secondary to reduced ileal absorptive capacity from ileal inflammation
- Reduced production of fibroblast growth factor 19 by enterocytes leading to increased hepatic bile acid synthesis
- Impaired lipid absorption secondary to immune-mediated duodenal villous atrophy
- Absence of the chloride-bicarbonate exchanger in the intestinal mucosa, causing cation and fluid retention

- E. Reduction of the total intestinal absorptive mucosal surface area leading to increased bile acid delivery to the colon

CORRECT ANSWER: B

RATIONALE

This patient meets Rome IV diagnostic criteria for irritable bowel syndrome-diarrhea predominant ([IBS-D]; recurrent abdominal pain related to defecation with associated change in stool frequency and form with more than 25% of bowel movements with Bristol stool form types of 6 or 7). Supportive testing is negative for common alternative diagnoses including a normal C-reactive protein and fecal calprotectin (rules out IBS), tissue transglutaminase antibody (TTG; rules out Celiac disease), and hemoglobin. Her diagnostic testing is most notable for an elevated 48-hour total fecal bile acid, which is consistent with bile acid malabsorption (BAM), specifically Type II idiopathic BAM with no clear underlying pathologic etiology. BAM is thought to have an estimated prevalence of 30% in patients with functional diarrhea or IBS-D.

Four types of BAM are recognized, including Type I (ileal disease, including inflammatory, surgical resection, and radiation-induced ileal disease), Type II (idiopathic, seen in functional diarrhea or IBS-D), Type III (malabsorption of bile acids secondary to alternative causes such as small intestinal bacterial overgrowth, chronic pancreatitis, postcholecystectomy or vagotomy, and Celiac disease), and Type IV (increased bile synthesis induced by treatment with metformin). The primary mechanism for Type II BAM is now considered to be related to reduced production of fibroblast growth factor 19 (FGF-19) by ileal enterocytes and resulting abnormal feedback inhibition of hepatic bile acid synthesis by FGF-19. FGF-19 is normally generated by ileal epithelial enterocytes cells in response to bile acid resorption. A defective and reduced production of FGF-19 leads to low fasting serum FGF-19 and reciprocally increases hepatic synthesis and

secretion of bile acids and leads to bile acid diarrhea. Low FGF-19 may be related to reduced messenger RNA expression in ileal enterocytes.

Bile acid malabsorption secondary to reduced ileal absorptive capacity from ileal inflammation (answer A) can be seen in Crohn's disease or radiation enteritis (Type I BAM), which is unlikely with this patient's negative C-reactive protein and fecal calprotectin. Impaired lipid absorption secondary to immune-mediated duodenal villous atrophy (answer C) would be expected in Celiac disease, not in this case due to negative TTG test. Absence of the chloride-bicarbonate exchanger in the intestinal mucosa (answer D) is seen in congenital chloridorrhea and is unlikely here. Reduction of the total intestinal absorptive mucosal surface area (answer E) can be seen in patients with a history of small bowel resection, especially ileal resection, and is not relevant due to her lack of surgical history.

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- Vijayvargiya P, Camilleri M. Current Practice in the Diagnosis of Bile Acid Diarrhea. *Gastroenterology*. 2019;156(5):1233-1238. doi:10.1053/j.gastro.2018.11.069

Question 35

A 48-year-old man presents to the office for evaluation of diarrhea. He has a history of recently diagnosed Crohn's ileocolitis with ileal stricture and underwent an uncomplicated laparoscopic ileocectomy 6 months ago. He reports that since his surgery he has noticed 4 to 6 loose, watery nonbloody (Bristol Stool Scale, 6) bowel movements daily. He has several more bowel movements in the morning, which seem to slow as the day progresses. There is a general association with meals, but he cannot identify a specific food trigger. He denies bleeding, weight loss, abdominal pain, nausea, vomiting, abdominal distension or bloating, or nocturnal stools. He completed 3 months of metronidazole after his surgery but is not currently receiving any medications. His only prior Crohn's treatment was intermittent prednisone until his surgery.

Physical examination reveals well-healed laparoscopy scars without tenderness or distension and normoactive bowel sounds. Colonoscopy reveals a normal post-operative anatomy with a healthy ileocolonic anastomosis, no ulcers (Rutgeerts, 10), no stenosis, and normal-appearing colonic mucosa. Histology reveals inactive chronic ileitis and normal colonic mucosa. Glucose hydrogen breath test reveals an increase in baseline hydrogen by 10 ppm after 90 minutes. Stool for *Clostridium difficile* toxins A and B is negative.

Which of the following is most likely to effectively treat the cause of this patient's diarrhea?

- A. Infliximab
- B. Cholestyramine
- C. Pancreatic enzyme replacement therapy
- D. Rifaximin
- E. Budesonide

CORRECT ANSWER: B

RATIONALE

This patient's clinical scenario is most consistent with Type I bile acid malabsorption (BAM) as

a consequence of his recent ileocecal resection. Active ileal disease or ileal resection, by way of a reduced bile acid absorptive capacity, will result in relatively excessive amounts of bile acid to enter the colon. Excessive colonic load of bile acid induces a cholerrheic diarrhea via several mechanisms, including stimulation of intracellular mediators, increased intestinal permeability, and enteroendocrine and neurocrine mechanisms. The net result is a secretory diarrhea from increased colonic motility and secretion of chloride, fluid and mucous and reduced sodium and water absorption. Due to limited diagnostic test availability for BAM, such as 75-Selenium homotaurocholic acid nuclear medicine scan, total 48-hour stool bile acid measurement, or serum fibroblast growth factor 19, it is reasonable to treat empirically with bile acid binders if BAM is suspected and follow for clinical improvement to suggest BAM as the cause for diarrhea.

This patient's colonoscopy was negative for post-operative recurrence of his Crohn's disease or microscopic colitis; therefore, infliximab (answer A) and budesonide (answer E) are unlikely to treat the cause of his symptoms. His glucose hydrogen breath test is negative (<20 ppm above baseline within 90 minutes) and his symptoms are not consistent with irritable bowel syndrome-diarrhea predominant (IBS-D); therefore, rifaximin is unlikely to treat the cause of his symptoms. Finally, although testing for exocrine pancreatic insufficiency was not performed (answer C), this is much less likely to be a cause of diarrhea in this post-ileal resection patient compared with BAM, though testing can be considered if symptoms do not respond to bile binding treatment.

REFERENCES

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Question 36

A 52-year-old woman presents in hospital consultation with 2 weeks of diarrhea. She has a history of acute myeloid leukemia and underwent an allogenic hematopoietic stem cell transplantation (HSCT) approximately 2 weeks ago. She reports frequent watery nonbloody (Bristol Stool Scale, 7) bowel movements at least 10 to 12 times daily for the past 3 days, including 2 to 3 nocturnal stools. There is associated abdominal cramping with most bowel movements and some nausea without vomiting. She reports oral pain and blistering. Her appetite is diminished, and she has lost about 5 pounds since symptoms began. Abdominal examination reveals mild diffuse tenderness without rebound or guarding and mildly hyperactive bowel sounds. Oropharyngeal examination reveals mucositis with aphthae.

Clostridium difficile stool toxins A and B via enzyme immunoassay are negative. Computed

tomography of the abdomen and pelvis is notable for diffuse mild thickening of the colon with mucosal hyperenhancement.

Initial laboratory test results are below.

Which of the following endoscopic and histologic findings would be expected in this patient?

- A. Normal colonic mucosa and histologic thickened sub-epithelial collagen band
- B. Terminal ileal ulcerations with histologic paneth cell metaplasia and noncaseating granulomas
- C. Colonic pale-yellow raised plaques with histologic necrotic epithelium and active acute neutrophilic colitis
- D. Colonic mucosa with diffuse moderate erythema, loss of vascularity, friability and erosions from rectum to cecum, and histologic chronic active colitis with crypt abscess and architectural distortion

Patchy rectal mucosal edema and erythema and rectal histologic epithelial cell apoptosis and necrotic crypts

CORRECT ANSWER: E

RATIONALE

This patient’s clinical presentation is most consistent with acute lower gastrointestinal graft-vs-host disease (GvHD). The clinical presenta-

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	102	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	84	10-40
Bilirubin, serum		
Total, mg/dL	1.4	0.3-1.0
Direct, mg/dL	1.0	0.1-0.3
Indirect, mg/dL	0.4	0.2-0.7
C-reactive protein, mg/dL	2.8	≤0.8
Hematocrit, blood, %	24	37-47
Hemoglobin, blood, g/dL	7.4	12-16
Platelet count, PLT/μL	80,000	150,000-450,000
White blood count (WBC) THOU/uL	2.6	4.2 - 9.1

tion of lower gastrointestinal (GI) GvHD can be variable; however, it most commonly presents as lower abdominal pain and diarrhea in patients after allogeneic HSCT. The secretory diarrhea can be severe and most commonly presents within a few weeks after HSCT, though can occur at any time after transplant. Evaluation requires clinical suspicion, ruling out other common causes of symptoms (medications, infectious etiology) and confirmatory testing. Since clinical, biochemical, and radiographic findings can be nonspecific, histologic confirmation via colonoscopy or sigmoidoscopy with biopsy is preferred when clinical suspicion is high. Upper endoscopy with gastroduodenal biopsies can also be considered, particularly in patients with upper GI symptoms (nausea, anorexia, dyspepsia). As biopsies from the distal colon and rectum are highly sensitive for detecting acute lower GI GvHD, a flexible sigmoidoscopy is often preferred in these patients due to safety, ease of performance, and lack of bowel preparation requirement. Endoscopic findings are often nonspecific and can range from normal-appearing mucosa to mild edema, erythema, aphthae, erosions, ulcerations, denuded mucosa, and bleeding. Histopathologic diagnosis is critical, revealing epithelial cell apoptosis with apoptotic bodies, as well as loss of crypts and crypt necrosis.

The alternative answer choice representing microscopic collagenous colitis (answer A), Crohn's disease of the ileum (answer B), pseudomembranous colitis (answer C), and ulcerative colitis (answer D) are all unlikely in this clinical scenario.

REFERENCE

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Question 37

A 54-year-old man presents for evaluation of diarrhea. He reports several years of intermittent diarrhea with 4 to 6 greasy appearing and foul-smelling stools daily. He notes associated abdominal cramping and epigastric discomfort, bloating, and gas. He has lost approximately 15 pounds over the past year as symptoms have progressed. The diarrhea tends to be worse after a particularly fatty meal. He denies nocturnal stooling, bleeding, nausea, vomiting, jaundice, recent travel, or antibiotic exposure. He has a history of alcohol abuse in remission for the past 3 years and is an active smoker with a 50 pack-year history. He does not take any medications. He had a normal screening colonoscopy at age 50. Physical examination reveals mild epigastric tenderness without rebound or guarding and normoactive bowel sounds. Computed tomography (CT) scan of the abdomen and pelvis reveals a mildly dilated pancreatic duct with scattered pancreatic calcification and no evidence of mass lesion. Initial laboratory test results are shown below.

Which of the following is the next best diagnostic test to perform for this patient?

Laboratory Test	Result	Reference Range
25-Hydroxyvitamin D (25-hydroxycholecalciferol), serum, ng/mL	8	20-60
Albumin, serum, g/dL	4.0	3.5-5.5
C-reactive protein, mg/dL	1.2	≤0.8
Glucose, plasma (fasting), mg/dL	206	70-99
Hematocrit, blood, %	42	42-50
Hemoglobin, blood, g/dL	14	14-18
Mean corpuscular volume, fL	102	80-98
Tissue transglutaminase antibody, IgA, serum, U/mL	<0.5 (Normal total IgA)	<4.0 (Negative)

- A. Upper endoscopy with duodenal biopsies
- B. Colonoscopy with random colonic biopsies
- C. Fecal pancreatic elastase measurement
- D. Stool studies for *Giardia* antigen and ova and parasites
- E. Stool alpha-1 antitrypsin measurement

CORRECT ANSWER: C

RATIONALE

This patient's risk factors (chronic smoking and alcohol use) along with malabsorption (steatorrhea, fat-soluble vitamin deficiencies), make chronic pancreatitis (CP) with exocrine pancreatic insufficiency (EPI) the most likely diagnosis. Supportive clues include CT finding with dilated pancreatic duct and pancreatic calcifications without a mass and hyperglycemia. Although several direct and indirect tests are available for evaluation of pancreatic function, all with advantages and disadvantages, fecal pancreatic elastase tends to be readily available, easily obtainable, and non-invasive and is therefore often a preferred initial diagnostic test in patients with suspected EPI. Additional testing options include cholecystokinin stimulation test, secretin stimulation test, serum trypsinogen/trypsin and fecal chemotrypsin test, and ¹³C-mixed triglyceride test. Therapeutic trial of pancreatic enzyme replacement therapy (PERT) is suggested in patients with EPI and evidence for fat malabsorption, and it can have both diagnostic and therapeutic value. In fact, in patients with known CP who present with signs and symptoms of malabsorption, a positive response to a trial of PERT alone without additional testing may be sufficient for a diagnosis of EPI.

Upper endoscopy with duodenal biopsies (answer A) would be performed if there was suspicion for Celiac disease; however, this patient had a negative ttg making that diagnosis unlikely. Colonoscopy with random colonic biopsies (answer B) would be useful to evaluate for microscopic colitis, which is unlikely in this patient given the steatorrhea and CT findings. Similarly, stool testing for *Giardia* antigen and ova and parasites (answer D)

and for protein-losing enteropathy (answer E) is not the best answer as patient lacks risk factors and historical characteristics for chronic parasitic infection (no travel) or protein-losing enteropathy (normal serum albumin).

REFERENCE

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Question 38

A 54-year-old woman presents to your office with chronic diarrhea. She reports several years of watery, nonbloody, painless diarrhea (Bristol Stool Scale, 7) approximately 6 to 8 times daily. She denies antibiotic exposure, travel history, weight loss, nausea, vomiting, abdominal pain, bleeding, or jaundice. There is no change in symptoms with food, and she occasionally experiences 1 to 2 nocturnal stools and mild fecal incontinence. She has a history of type 1 diabetes mellitus complicated by peripheral neuropathy and retinopathy. She denies alcohol and tobacco use. Her medications include subcutaneous insulin, aspirin, and atorvastatin. Physical examination reveals a body mass index of 29, normal vital signs, soft nontender nondistended abdomen with normoactive bowel sounds, and reduced sensation of both lower extremities to filament testing.

Colonoscopy reveals normal mucosa, and random biopsies from the right and left colon are normal. A lactose hydrogen breath test reveals an increase in hydrogen by 5 ppm over baseline over 120 minutes, and a glucose hydrogen breath test reveals an increase in hydrogen by 2 ppm over baseline over 90 minutes. Stool testing is negative for *Clostridium difficile* toxin A and B and *Giardia* antigen. Initial blood work results shown on the following page.

Which of the following is the most likely pathophysiologic mechanism for this patient's diarrhea?

Laboratory Test	Result	Reference Range
C-reactive protein, mg/dL	2.0	≤0.8
Creatinine, serum, mg/dL	2.2	0.7–1.5
Ferritin, serum, ng/mL	300	11–211
Glucose, plasma (fasting), mg/dL	280	70–99
Hematocrit, blood, %	35	37–47
Hemoglobin A1C, %	11.2	4.0–5.6
Hemoglobin, blood, g/dL	11	12–16
Tissue transglutaminase antibody, IgA, serum, U/mL	<0.5 (Normal total IgA)	<4.0 (Negative)
Thyroid-stimulating hormone (TSH), serum, μ U/mL (mU/L)	2.4	0.5–4.0 (0.5–4.0)

- A. Autonomic and enteric nervous system dysregulation leading to altered intestinal fluid and electrolyte absorption and dysmotility
- B. Increased concentration of osmotically active small bowel luminal contents leading to luminal osmotic fluid shifts
- C. Colonic mucosa with increased lamina propria lymphocytes resulting in altered tight junctions and alterations in ion transportation
- D. Bacterial-induced enterocyte damage leading to intestinal maldigestion of carbohydrates and lipids
- E. Antigen-derived immune response leading to small bowel villous atrophy and subsequent malabsorption

CORRECT ANSWER: A

RATIONALE

This patient's diarrhea is best classified as diabetic diarrhea. Supportive clues in this case include clinical symptom characterization, long-standing poorly controlled insulin-dependent diabetes with neuropathy, and continued high glucose levels, as well as exclusion of other common causes of diarrhea in patients with diabetes. Diabetic diarrhea is a chronic watery painless diarrhea that can occur at night, can include alternating bowel habits, and can be concurrent with fecal incontinence or symptoms of gastroparesis. Diagnosis is generally made in the appropriate clinical setting (long-standing insulin-dependent diabetes with

poor glycemic control and neuropathy) and with exclusion of other etiologies for diarrhea. Common alternative etiologies of diarrhea to rule out in diabetics include medications (metformin being most common), infection, Celiac disease, microscopic colitis or inflammatory bowel disease, small intestinal bacterial overgrowth, disaccharide intolerance, and other endocrine disorders.

The pathophysiology of diabetic diarrhea is complex. However, multiple factors likely contribute, including autonomic and enteric nervous system dysregulation leading to altered motility, abnormal mucosal fluid and electrolyte secretion or absorption, and disruptions to the epithelium. This patient's case is not suggestive of lactose intolerance (answer B) due to negative lactose breath test, microscopic colitis (answer C) due to normal colonic histology, small intestinal bacterial overgrowth (answer D) due to negative glucose hydrogen breath test, nor Celiac disease (answer E) due to negative ttg. Her mild anemia with elevated ferritin and C-reactive protein is likely suggestive of anemia of chronic disease from poorly controlled diabetes. This patient also has mild diabetic-related chronic kidney insufficiency.

REFERENCE

Selby A, Reichenbach ZW, Piech G, Friedenber FK. Pathophysiology, Differential Diagnosis, and Treatment of Diabetic Diarrhea. *Dig Dis Sci*. 2019;64(12):3385–3393. doi:10.1007/s10620-019-05846-6

Laboratory Test	Result	Reference Range
Aminotransferase, serum alanine (ALT, SGPT), U/L	12	10–40
Aminotransferase, serum aspartate (AST, SGOT), U/L	14	10–40
Bilirubin, serum		
Total, mg/dL	0.8	0.3–1.0
Direct, mg/dL	0.2	0.1–0.3
Indirect, mg/dL	0.6	0.2–0.7
C-reactive protein, mg/dL	0.8	≤0.8
Ferritin, serum, ng/mL	10	20–235
Hematocrit, blood, %	36	42–50
Hemoglobin, blood, g/dL	12	14–18
Mean corpuscular volume, fL	76	80–98
Platelet count, PLT/ μ L	320,000	150,000–450,000
Thyroid-stimulating hormone (TSH), serum, μ U/mL (mU/L)	3.2	0.5–4.0 (0.5–4.0)
Tissue transglutaminase antibody, IgA, serum, U/mL	<0.5 (Normal total IgA)	<4.0 (Negative)

Question 39

A 44-year-old man presents to the office with 4 months of diarrhea. He reports prior normal bowel habits until about 4 months ago when he developed 3 to 4 loose nonbloody stools (Bristol Stool Scale, 6) daily. There is associated abdominal bloating and lower abdominal cramping. He has lost about 5 pounds during this time, which he attributes to generally feeling unwell. He denies fever, nausea, vomiting, recent travel or antibiotic exposure. His family history is relevant for a mother with endometrial cancer at age 42. Physical examination reveals conjunctival pallor, hyperactive bowel sounds, no tenderness or distension. Stool testing for *Clostridium difficile* toxin A and B antigen, ova and parasites, and Giardia antigen is negative.

Initial laboratory test results are shown above.

Which of the following is the next best step in evaluation of this patient?

- A. Upper endoscopy with duodenal biopsies
- B. Colonoscopy
- C. Fecal calprotectin measurement
- D. Magnetic resonance enterography
- E. Lactose hydrogen breath test

CORRECT ANSWER: B

RATIONALE

This patient's clinical scenario with recent change in bowel habits associated with iron deficiency anemia is concerning for possible colonic neoplasia; therefore, a colonoscopy is the next best step in the diagnostic evaluation. Other concerning clues are his family history of endometrial cancer at a young age, which could raise suspicion for Lynch syndrome. In the presence of alarm signs or symptoms, such as bleeding, weight loss, or iron deficiency anemia, further evaluation is necessary, in this case a colonoscopy.

This patient has a negative Celiac screen; therefore, upper endoscopy with duodenal biopsies (answer A) alone is not the preferred next step in evaluation, although upper endoscopy is often combined with colonoscopy to evaluate iron deficiency anemia. Fecal calprotectin (answer C) is commonly used to evaluate patients suspected of having an inflammatory etiology for diarrhea or to rule out inflammatory diarrhea, and although that test might be appropriate to check in this patient, the iron deficiency anemia needs evaluation with colonoscopy. Magnetic resonance enterography (answer D) is used to evaluate small bowel disease and would not be the next best step before a colonoscopy to evaluate diarrhea with iron deficiency anemia. Lactose hydrogen breath test (answer E) is useful to evaluate for lactose intolerance but

Laboratory Test	Result	Reference Range
C-reactive protein, mg/dL	0.2	≤0.8
Fecal calprotectin, mcg/g	16	<50
Hematocrit, blood, %	42	37-47
Hemoglobin, blood, g/dL	14	12-16
Mean corpuscular volume, fL	90	80-98
Thyroid-stimulating hormone (TSH), serum, $\mu\text{U/mL}$ (mU/L)	2.4	0.5-4.0 (0.5-4.0)
Tissue transglutaminase antibody, IgA, serum, U/mL	<0.5 (Normal total IgA)	<4.0 (Negative)

would not be recommended in evaluation of diarrhea with iron deficiency anemia.

REFERENCE

Ko CW, Siddique SM, Patel A, et al. AGA Clinical Practice Guidelines on the Gastrointestinal Evaluation of Iron Deficiency Anemia. *Gastroenterology*. 2020;159(3):1085-1094. doi:10.1053/j.gastro.2020.06.046

Question 40

A 20-year-old woman presents to the office for evaluation of chronic diarrhea. She reports that since childhood, she has alternating but predominantly loose stool (Bristol Stool Scale, 5-6) 3 to 6 times daily. She reports that she has diarrhea approximately 75% of the time, and more normal formed stools 25% of the time. She has associated abdominal discomfort described as generalized cramping and mild pain that tends to improve with bowel movements. Symptoms do sometimes worsen with stress from work. She denies bleeding, weight loss, nausea, vomiting, recent travel, or antibiotic exposure, or association with food. She takes no medications other than occasional loperamide as needed for diarrhea, and there is no family history of colon cancer, celiac disease, or inflammatory bowel disease. Physical examination is unremarkable.

Initial laboratory test results are shown above.

Which of the following is the best next step in diagnostic evaluation?

- A. Upper endoscopy with duodenal biopsies
- B. Colonoscopy with random colonic biopsies
- C. Stool testing for *Clostridium difficile* toxin A and B antigen, ova, and parasites
- D. Glucose hydrogen breath test
- E. No additional diagnostic testing necessary

CORRECT ANSWER: E

RATIONALE

This patient's clinical scenario is most consistent with irritable bowel syndrome-diarrhea predominant (IBS-D). She meets Rome IV criteria with recurrent abdominal pain, on average, at least 1 day weekly in the last 3 months, associated with 2 or more criteria of relation to defecation, change in stool frequency and/or stool form. The diarrhea subtype requires more than 25% of bowel movements with Bristol stool form types 6 or 7 and less than 25% of bowel movements with Bristol stool form types 1 or 2.

In the absence of alarm signs or symptoms, basic limited selective testing is suggested in patients fulfilling diagnostic criteria for IBS-D to rule out common disorders with similar symptoms. Generally, patients should be evaluated with noninvasive testing, including laboratory testing for Celiac disease, anemia, and inflammatory diarrhea (C-reactive protein/fecal calprotectin). Testing for thyroid dysfunction and stool enteric infectious pathogens can be considered in patients with risk factors or with specific clinical concerns. Provided initial selective testing is negative, a positive diagnostic strategy confirming IBS as the diagnosis

and initiation of directed treatment is then preferable to a diagnostic strategy of exclusion with additional testing for patients with typical IBS symptoms. Providers should avoid performing unnecessary testing in patients with definite IBS-D and negative basic initial testing, such as unnecessary colonoscopy or endoscopy. Patients who do not respond to directed IBS treatment can then be evaluated further as clinically necessary.

This patient has a normal ttg, C-reactive protein, and fecal calprotectin, so an endoscopy and colonoscopy are very low diagnostic yield and are unnecessary at this time (answers A and B). Routine stool testing for enteric pathogens is generally unnecessary and not recommended in patients with IBS-D except those with a high pretest probability and risk factors for specific pathogen exposure (answer C), which this patient lacks. This patient does not have specific risk factors for small intestinal bacterial overgrowth; therefore, it is not necessary to perform glucose hydrogen breath testing at this time (answer D).

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Schiller LR, Pardi DS, Sellin JH. Chronic Diarrhea: Diagnosis and Management. *Clin Gastroenterol Hepatol*. 2017;15(2):182-193.e3. doi:10.1016/j.cgh.2016.07.028

Question 41

A 64-year-old woman presents to your office to evaluate chronic diarrhea. She reports approximately 2 years of nonbloody diarrhea. She reports

variable 4 to 6 loose bowel movements daily (Bristol Stool Scale, 6) with associated nausea and diminished appetite. She has intermittent abdominal pain described as a diffuse lower and central abdominal cramping discomfort that is not necessarily associated with bowel movements. She denies weight loss, bleeding, recent travel, or antibiotic history. Her medical history is significant for cervical cancer treated with concurrent chemoradiation therapy completed 5 years ago. She does not take any medications and denies nonsteroidal antiinflammatory drug use. Family history is negative for gastrointestinal malignancy or inflammatory bowel disease. Physical examination reveals a body mass index of 18 kg/m², normal vital signs, and abdominal examination with mild abdominal distension, mild lower abdominal tenderness without rebound or guarding, and hyperactive bowel sounds.

Computed tomography of the abdomen and pelvis with contrast reveals several pelvic loops of small bowel with bowel wall thickening, mucosal hyperenhancement, mesenteric stranding, and mild dilation proximally. Colonoscopy is notable for a normal-appearing colon with normal histology, and the terminal ileum shows contiguous edema, pallor with friability, and serpiginous telangiectasias with a fibrotic appearing stricture. Ileal histology is notable for inflammatory infiltrate with arteriolar intimal proliferation, submucosal fibrosis, and vascular sclerosis and vasculitis.

Laboratory test results on the following page.

Which of the following is the most likely primary pathophysiologic mechanism for this patient's diarrhea?

- A. Antigen-derived immune response leading to small bowel villous atrophy and subsequent nutrient malabsorption
- B. Free radical enterocyte cell damage, capillary fibrosis, chronic ischemia, and obliterative arteritis causing secondary bile acid malabsorption and small intestinal bacterial overgrowth

Laboratory Test	Result	Reference Range
C-reactive protein, mg/dL	3.6	≤0.8
Hematocrit, blood, %	33	37-47
Hemoglobin, blood, g/dL	11	12-16
Mean corpuscular volume, fL	72	80-98
Tissue transglutaminase antibody, IgA, serum, U/mL	<0.5 (Normal total IgA)	<4.0 (Negative)

- C. Dysregulated immune response to luminal bacteria and antigens leading to chronic progressive inflammatory bowel damage, altered intestinal microbiota, and malabsorption
- D. Abnormal enteric nervous system alteration of intestinal fluid and electrolyte absorption and dysmotility leading to rapid transit of increased colonic water volumes
- E. Aberrant cellular and humoral immune activity leading to endothelial dysfunction and cellular infiltrate with perivascularitis, phlebitis and venous thrombosis leading to malabsorption

CORRECT ANSWER: B

RATIONALE

This patient's clinical, radiographic, endoscopic, and histologic findings are most consistent with chronic radiation enteritis. Chronic radiation enteritis occurs in patients with a history of abdominal or pelvic radiation, often months to years after treatment is completed. This clinical presentation is variable depending upon the involved areas of bowel and severity of tissue injury, but can include abdominal pain, diarrhea, malabsorption, weight loss, bleeding, and sequela of bowel strictures and chronic inflammation including fistula. Diarrhea is one of the most common presenting symptoms. Diagnosis is made in the proper clinical context of a radiation therapy history with supportive symptoms, including radiographic, endoscopic, and histologic findings. Imaging findings are often nonspecific and can show small bowel and colonic inflammatory changes, strictures, and fistula. Endoscopic findings are nonspecific and can show edema, erythema, ulcerations, fibrosis, and telangiectasias. Histologic findings often include inflammatory infiltrate with arteriolar intimal pro-

liferation, submucosal fibrosis, collagen deposition, and vascular sclerosis and vasculitis.

The primary pathophysiologic insult is due to direct and indirect enterocyte damage from direct ionizing radiation and free radicals. This ultimately leads to apoptosis, capillary fibrosis, chronic ischemia and obliterative arteritis. Patients with chronic radiation enteritis are then subject to multiple secondary complicating sequela due to enterocyte and structural bowel damage that cause symptoms, including bile acid malabsorption, small intestinal bacterial overgrowth, carbohydrate malabsorption, and dysmotility.

Answer A represents Celiac disease, which is inconsistent with this patient's presentation. Answer C represents pathophysiology of inflammatory bowel disease, which is unlikely given this patient's history. Answer D represents changes seen with irritable bowel syndrome, which is not the correct diagnosis in this case. Answer E represents the suspected pathophysiology of Behcet's syndrome.

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Question 42

A 72-year-old man presents to the office for evaluation of 3 weeks of diarrhea. He reports no prior gastrointestinal symptoms until he developed 5 to 7 loose watery nonbowel movements daily about 3 weeks ago after visiting his primary care doctor. He denies abdominal pain, bleeding, recent travel, or antibiotic exposure. He cannot associate the symptoms to meals or particular food. His family history is notable for a nephew with Crohn's disease and a granddaughter with celiac disease. His medications include amlodipine for hypertension and colchicine for gout after a recent flare did not respond to nonsteroidal anti-inflammatory drugs. Physical examination is remarkable for body mass index of 32 kg/m², blood pressure of 124/72 mmHg, and abdominal examination with obese abdomen without tenderness and normoactive bowel sounds.

Which of the following is the best next step?

- A. Switch amlodipine to alternative anti-hypertensive therapy
- B. Stop colchicine and monitor clinically for symptom improvement
- C. Evaluate stool sample for *Clostridium difficile* toxin A and B antigen and ova and parasites
- D. Test Fecal calprotectin, blood C-reactive protein, and anti-tissue transglutaminase IgA levels
- E. Start psyllium

CORRECT ANSWER: B

RATIONALE

This patient's acute diarrhea without alarm signs or symptoms is most likely due to medication, specifically colchicine used to treat acute flares of gout. Diarrhea is one of the most common side effects of colchicine. Colchicine-induced diarrhea occurs via multiple mechanisms including secretory diarrhea from the inhibition of Na/K-ATPase activity and interference with the migration of epithelial cells, as well as villous atrophy and mal-

absorption. There tends to be a dose-dependent effect particularly when taken at high doses. A careful and thorough history is critical to the diagnosis of drug-induced diarrhea, and the majority of the time diarrhea will resolve within several days of medication cessation.

Answer A is incorrect as amlodipine tends to cause constipation, and colchicine is the more likely culprit for the symptoms. Answers C, D, and E are incorrect as it is not necessary to test for infectious or inflammatory causes if there are no specific risk factors or historic elements to suggest these processes and if the more likely cause is medication-induced diarrhea based upon history. Further evaluation can be considered if symptoms do not improve after cessation of the offending medication.

REFERENCE

Abraham BP, Sellin JH. Drug-induced, factitious, & idiopathic diarrhoea. *Best Pract Res Clin Gastroenterol.* 2012;26(5):633-648. doi:10.1016/j.bpg.2012.11.007

Question 43

A 78-year-old man presents to the office with 6 months of diarrhea. He reports loose, fatty appearing nonbloody stool (Bristol Stool Scale, 6) at least 6 to 8 times daily for the past 6 months. There is no abdominal pain, fever, nausea, vomiting, bloating, bleeding, recent travel, sick contacts, or antibiotic exposure. He has lost about 20 pounds since this time. He also reports fatigue and generalized weakness and some numbness of his toes. His medical history includes multiple myeloma and hyperlipidemia. Physical examination reveals normal vital signs and mild bibasilar crackles on lung examination. Abdominal examination notes a soft, nontender, nondistended abdomen with normoactive bowel sounds, with mild hepatomegaly appreciated. There is mild lower extremity edema.

Initial laboratory test results are shown on the following page.

Laboratory Test	Result	Reference Range
Alkaline phosphatase, serum, U/L	302	30-120
Aminotransferase, serum alanine (ALT, SGPT), U/L	78	10-40
Aminotransferase, serum aspartate (AST, SGOT), U/L	102	10-40
Bilirubin, serum		
Total, mg/dL	0.8	0.3-1.0
Direct, mg/dL	0.2	0.1-0.3
Indirect, mg/dL	0.6	0.2-0.7
Blood urea nitrogen (BUN), serum or plasma, mg/dL	42	8-20
C-reactive protein, mg/dL	1.8	≤0.8
Creatinine, serum, mg/dL	2.2	0.7-1.5
Hematocrit, blood, %	36	42-50
Hemoglobin, blood, g/dL	12	14-18

Which of the following is the most likely diagnostic finding to explain this patient's diarrhea?

- A. Upper endoscopy with duodenal biopsies showing periodic acid-Schiff staining-positive macrophages
- B. Percutaneous liver biopsy showing inflammatory periductular granulomatous bile duct lesion
- C. Double balloon enteroscopy with jejunal biopsies shows abundant monomorphic infiltrating lymphoid cells
- D. Colonoscopy with random colorectal and ileal biopsies showing apple-green birefringence on Congo red staining
- E. Flexible sigmoidoscopy with rectal biopsies showing epithelial cell apoptosis and necrotic crypts

CORRECT ANSWER: D

RATIONALE

This patient's overall clinical presentation should raise suspicion for gastrointestinal (GI) and hepatic amyloidosis given his history of multiple myeloma, cholestatic liver abnormalities, hepatomegaly, anemia, and renal insufficiency. Amyloidosis is an uncommon condition characterized by multi-organ extracellular tissue deposit of protein fibrils. Due to the potential to involve multiple organ systems, the symptoms are highly variable and high clinical suspicion is required in the proper context. The most common form

is primary amyloidosis secondary to light chain deposition, generally seen in patients with light chain disorders such as multiple myeloma (such as in this patient). GI and hepatic amyloid deposition can lead to a variety of signs and symptoms, such as diarrhea, weight loss, GI bleeding, anemia, abnormal liver enzymes generally infiltrative or cholestatic pattern, dysmotility with rapid transit time, and hepatomegaly. Diarrhea may be related to a combination of mechanisms including direct mucosal fibril deposition, dysmotility due to neuromuscular fibril deposition, protein-losing enteropathy, bile acid malabsorption, small intestinal bacterial overgrowth, and/or pancreatic insufficiency. When clinical suspicion is high for GI amyloidosis, upper endoscopy and/or colonoscopy is recommended to rule out other etiologies and obtain tissue samples, especially from the rectum and small bowel. A liver biopsy can be obtained in patients with suspected hepatic amyloidosis to confirm diagnosis and evaluate for alternative etiologies for abnormal liver enzymes. Histologic confirmation is made with Congo red staining producing a characteristic apple-green birefringence under polarized light.

Answer A represents expected findings in patients with Whipple's disease, classically presenting with diarrhea, abdominal pain, joint pain, and neurologic abnormalities. Answer B represents findings of primary biliary cholangitis, which can lead to fat malabsorption and steatorrhea. Answer C would be expected in a patient with small

bowel lymphoma. Answer E would be findings in a patient with GI graft-vs-host disease.

REFERENCE

Ebert EC, Nagar M. Gastrointestinal manifestations of amyloidosis. *Am J Gastroenterol*. 2008;103(3):776-787. doi:10.1111/j.1572-0241.2007.01669.x

Question 44

A 68-year-old woman presents for evaluation of chronic diarrhea. She reports about 3 months of loose non-bloody stools (Bristol Stool Scale, 7) up to 10 to 14 times daily. The diarrhea occurs with any oral intake including food and liquid without specific dietary triggers identified. The stool tends to float and is foul smelling with associated gas and bloating. She has lost 20 pounds during this time. She denies blood in the stool, recent travel, antibiotic exposure, abdominal pain, nausea, or vomiting. She was seen by her primary care doctor for several months to attempt to manage mild diarrhea; however, due to worsening symptoms she was referred to you. She has a history of coronary and peripheral artery disease with claudication. One year ago, she developed acute mesenteric ischemia and underwent emergent small bowel resection with an approximately 120 cm of distal small bowel removed. Her current medications include aspirin, atorvastatin, metoprolol, omeprazole, cholestyramine, loperamide, and rivaroxaban. Initial evaluation with colonoscopy noted normal-appearing colon and normal histology. Lactose hydrogen breath test reveals an increase in breath hydrogen by 8 ppm at 90 minutes.

Which of the following is the most likely pathophysiology for this patient's worsened diarrhea?

- A. Reduction in total bile salt pool leading to fat malabsorption and steatorrhea
- B. Small bowel villous atrophy leading to malabsorption
- C. Osmotically active substances in the small bowel leading to osmotic diarrhea

- D. Leaky colonic tight junctions leading to secretory diarrhea
- E. Exocrine pancreatic enzyme deficiency leading to fat malabsorption and steatorrhea

CORRECT ANSWER: A

RATIONALE

This patient's clinical scenario is most suggestive of short bowel syndrome (SBS) after a catastrophic small bowel vascular event that required a significant small bowel resection. Patients with SBS have many possible etiologies of diarrhea. However, one often overlooked etiology is secondary to reductions in the bile salt pool leading to steatorrhea from fat malabsorption. Particularly, patients with over 100 cm of distal (ileal) small bowel removed are prone to worsening diarrhea and steatorrhea when started on bile acid sequestrant like cholestyramine due to worsening depletion of an already reduced bile acid pool related to reduced enterohepatic bile acid circulation from ileal resection. Therefore, bile acid sequestrants are not recommended in patients with SBS and over 100 cm of small bowel resected.

Answer B would be seen in celiac disease and is incorrect, as it is unlikely she has now developed celiac disease and there would be an expected intestinal adaptation with villous lengthening. Answer C is incorrect: though patients with SBS may develop carbohydrate malabsorption, it does not explain her worsening symptoms on cholestyramine and her negative lactose breath test. Answer D is incorrect as her colonoscopy is normal and there is no suggestion of colonic disease-causing diarrhea. Answer E is incorrect, though patients with SBS can have pancreatic insufficiency, particularly if not receiving enteral or oral diet (total parenteral nutrition-dependent), the more likely explanation in this patient is cholestyramine use in setting of SBS.

REFERENCES

American Gastroenterological Association.
American Gastroenterological Association medical position statement: short bowel syndrome

and intestinal transplantation. *Gastroenterology*. 2003;124(4):1105-1110. doi:10.1053/gast.2003.50139

Buchman AL, Scolapio J, Fryer J. AGA technical review on short bowel syndrome and intestinal transplantation. *Gastroenterology*. 2003;124(4):1111-1134. doi:10.1016/s0016-5085(03)70064-x

Question 45

A 20-year-old woman who is a nurse presents to the office for evaluation of chronic diarrhea. She reports 1 year of loose nonbloody diarrhea (Bristol Stool Scale, 7) up to 10 to 12 times daily and 1 to 2 bowel movements at night. There is associated abdominal cramping, and she has lost 15 pounds over the past 6 months. She denies nausea, vomiting, recent travel, or antibiotic exposure. Family history is negative for celiac disease or inflammatory bowel disease. She has had an extensive evaluation with 2 other gastroenterologists, an endocrinologist, a rheumatologist, and her primary care physician, including normal upper endoscopy and ileocolonoscopy with normal gastric, duodenal, ileal and colonic biopsies, negative stool for enteric pathogens, ova and parasites, normal abdominal-pelvic CT scan with contrast, negative lactose and glucose hydrogen breath testing, and negative testing for thyroid disease and autoimmune markers. She has had multiple visits to the emergency department

with no acute etiology for her diarrhea identified. Laboratory test results are shown below.

Which of the following additional tests would most likely lead to the correct diagnosis in this patient?

- A. No additional testing required
- B. Serum for vasoactive intestinal peptide and chromogranin A
- C. Fecal calprotectin
- D. Scintigraphic evaluation with 23-seleno-25-homotaurocholic acid, selenium homocholic acid taurine (SeHCAT) test
- E. Stool screen for laxatives

CORRECT ANSWER: E

RATIONALE

The most likely etiology for this patient's diarrhea is osmotic diarrhea from magnesium laxative abuse. This patient has several red flags to suggest factitious diarrhea, including work in a health care setting, having seen multiple providers, high health care utilization, and extensive evaluation without a diagnosis found. Supportive evidence in this case includes a stool osmotic gap more than 100 and elevated stool magnesium. The next best step to identify the cause of diarrhea, given the high suspicion for factitious diarrhea from laxative abuse, would be to check a stool screen for osmotic and stimulant laxatives.

Laboratory Test	Result	Reference Range
C-reactive protein, mg/dL	0.6	≤0.8
Glucose, plasma (fasting), mg/dL	78	70-99
Hematocrit, blood, %	40	37-47
Hemoglobin, blood, g/dL	14	12-16
Mean corpuscular volume, fL	88	80-98
Potassium, serum, mEq/L	2.9	3.5-5.0
Stool osmolality, mOsm/kg	290	--
Stool sodium, mmol/L	40	--
Stool potassium, mmol/L	48	--
Stool magnesium, mEq/L	118	--
Stool phosphate, mmol/L	12	--
Stool osmolality, mOsm/kg	290	--
Tissue transglutaminase antibody, IgA, serum, U/mL	<0.5 (Normal total IgA)	<4.0 (Negative)

Answer A is incorrect as this patient requires additional testing for laxative abuse and it would be incorrect to assume she has irritable bowel syndrome and decline further testing. Answer B is incorrect because the patient has an osmotic diarrhea and checking serum for vasoactive intestinal peptide and chromogranin A would be correct for a secretory diarrhea evaluation. Answer C is incorrect as patient already had a normal colonoscopy and has osmotic diarrhea, so fecal calprotectin would not add anything useful to the diagnosis. Answer D is incorrect as she is unlikely to have bile acid malabsorption in this scenario with an osmotic diarrhea.

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Question 46

A 19-year-old man presents to your office for evaluation of diarrhea. He reports 2 days of watery nonbloody diarrhea (Bristol Stool Scale, 7) about 6 to 10 times daily. There is associated lower abdominal cramping, gas, and mild nausea. He is able to tolerate a bland diet without difficulty and is maintaining hydration with electrolyte sports

drinks. He works as a teaching assistant in a local daycare center. His sister had a similar illness last week and has since improved. He denies fever, chills, night sweats, rectal bleeding, weight loss, vomiting, recent travel, or antibiotic exposure. He has no medical history and does not take any medications. Physical examination reveals temperature of 37.2 °C, heart rate of 84 bpm, blood pressure of 118/68 mmHg, body mass index of 24 kg/m², and abdominal examination with hyperactive bowel sounds and without tenderness or distension.

Which of the following is the best next step in management of this patient?

- A. Stool sample for *Clostridium difficile* toxin enzyme immunoassay, enteric pathogen polymerase chain reaction panel, and ova and parasites
- B. Measurement of C-reactive protein, anti-tissue transglutaminase IgA, and fecal calprotectin
- C. Schedule a colonoscopy with random colonic biopsies
- D. Empiric treatment with oral azithromycin for 3 days
- E. Supportive care with oral hydration, diet as tolerated, and loperamide as needed

CORRECT ANSWER: E

RATIONALE

This patient presents with an acute diarrheal illness, most likely a self-limited viral gastroenteritis; therefore, he does not need further testing or treatment other than supportive care with oral hydration and anti-diarrheal medications as needed. The vast majority of acute diarrhea illness in North America is self-limited from an infectious process, namely viral or bacterial pathogens. This patient's work in a daycare setting and sick contact suggest that he most likely has a viral gastroenteritis that will likely be self-limited. He lacks the clinical presentation, signs or symptoms of inflammatory diarrhea, severe or persistent illness, and high-risk

factors for severe disease, travel, or dehydration. Therefore, stool testing for enteric pathogens and empiric antibiotics are unnecessary (answers A and D). Patients with travel-associated diarrhea, fever, bloody diarrhea (dysentery), persistent symptoms, or those at high risk for severe illness can be considered for stool microbiologic assessment and empiric or directed antibiotic therapy. A colonoscopy (answer C) is unnecessary for presumed infectious acute diarrhea and would only be considered should symptoms persist to rule out an alternative process. Answer B would be appropriate as part of evaluation of chronic diarrhea (>4 weeks).

REFERENCE

Riddle MS, DuPont HL, Connor BA. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults. *Am J Gastroenterol*. 2016;111(5):602-622. doi:10.1038/ajg.2016.126

Question 47

A 42-year-old woman presents for evaluation of diarrhea. She reports 4 months of mild loose non-bloody stools (Bristol Stool Scale, 6) about 3 to 4 times daily. The diarrhea is particularly worsened by greasy fatty foods. There is no associated abdominal pain, weight loss, nocturnal stool, fever, nausea, vomiting, travel, or antibiotic exposure. Her medical history is significant for hypertension treated with amlodipine and acute cholecystitis status after cholecystectomy 5 months ago. She denies a family history of celiac disease or inflammatory bowel disease. Physical examination reveals normal vital signs and an obese, soft, non-tender nondistended abdomen with well-healed laparoscopy scars. You place her on cholestyramine twice daily which markedly improves her symptoms at her follow-up visit.

Which of the following is the most likely mechanism for this patient's diarrhea?

- A. Reduced ileal bile acid resorptive capacity
- B. Idiopathic abnormal bile acid feedback

mechanism leading to increased hepatic bile acid synthesis

- C. Increased concentration of continuous bile acid entering the colon leading to cholerrheic diarrhea
- D. Medication-induced increased hepatic bile synthesis
- E. Osmotic fluid shifts within the colonic lumen leading to osmotic diarrhea

CORRECT ANSWER: C

RATIONALE

This patient's clinical scenario is most consistent with post-cholecystectomy diarrhea, which is categorized under type III bile acid malabsorption (BAM)/bile acid diarrhea. Type III BAM is associated with a wide variety of underlying conditions that can collectively affect bile acid absorption, production, or enterohepatic circulation, one of the most common being post-cholecystectomy diarrhea (5%-12% of patients after cholecystectomy). Although the primary mechanism is uncertain, diarrhea occurring after cholecystectomy is most likely the result of a slow continuous bile acid flow into the small bowel, which overcomes the ileal resorptive capacity, increasing colonic stool bile acid concentration and causing a subsequent cholerrheic diarrhea. Studies on post-cholecystectomy patients have shown a significantly increased fecal bile acid concentration compared with controls. Treatment with bile sequestrants is often used empirically and is quite successful. Answer A is Type I BAM related to primary ileal disease; answer B is Type II BAM related to idiopathic BAM often seen in irritable bowel syndrome (IBS); answer D is Type IV BAM described with metformin use; and answer E would represent osmotic diarrhea usually from carbohydrate intolerance in the setting of small bowel disaccharidase deficiency.

REFERENCE

Arlow FL, Dekovich AA, Priest RJ, Beher WT. Bile acid-mediated postcholecystectomy diarrhea. *Arch Intern Med*. 1987;147(7):1327-1329.

Camilleri M, Vijayvargiya P. The Role of Bile Acids in Chronic Diarrhea. *Am J Gastroenterol*. 2020;115(10):1596-1603. doi:10.14309/ajg.0000000000000696

Vijayvargiya P, Camilleri M. Current Practice in the Diagnosis of Bile Acid Diarrhea. *Gastroenterology*. 2019;156(5):1233-1238. doi:10.1053/j.gastro.2018.11.069

Question 48

A 52-year-old woman presents to your office for evaluation of diarrhea. She reports a 5-year history of loose non-bloody diarrhea (Bristol Stool Scale, 6) approximately 6 to 8 times daily. She reports associated abdominal bloating and visible distension along with increased gas production. She cannot associate the symptoms with any particular food. She has occasional nocturnal diarrhea. There is no rectal bleeding, weight loss, recent travel, or antibiotic exposure. She has a past medical history of systemic sclerosis and prior Billroth II gastrectomy for perforated gastric ulcer due to nonsteroidal anti-inflammatory drug use. She denies a family history of celiac disease or inflammatory bowel disease. Her last colonoscopy at age 50 was endoscopically normal to the terminal ileum. Physical examination reveals a thin woman with mild abdominal distention and hyperactive bowel sounds without tenderness.

Abdominal x-ray is notable for a nonspecific bowel gas pattern, no obstruction or ileus identified. Initial laboratory test results include:

Which of the following is the most likely cause of diarrhea in this patient?

- A. Immune-mediated duodenal villous atrophy leading to malabsorption and intestinal barrier disruption
- B. Increased colonic lamina propria lymphocytes secondary to nonsteroidal anti-inflammatory drug use leading to inflammatory secretory diarrhea
- C. Elevated colony forming units of small intestinal bacteria secondary to intestinal dysmotility leading to maldigestion and malabsorption
- D. Reduced ileal absorptive capacity secondary to inflammatory ileal disease leading to choleraic diarrhea
- E. Bacterial enterotoxin and cytotoxin production leading to mucosal inflammation and secretory diarrhea

CORRECT ANSWER: C

RATIONALE
This patient’s clinical presentation is most suggestive of small bowel bacterial overgrowth. This patient has well established high-risk factors for small intestinal bacterial overgrowth (SIBO) including systemic sclerosis and prior gastrointestinal surgery. Patients with these conditions are prone to development of SIBO via a combination of mechanisms including gastrointestinal dysmotility and stasis as well as hypochlorhydria. The most common presenting symptoms for SIBO include gas, bloating, abdominal distension, and chronic diarrhea. Additional supporting clues to

Laboratory Test	Result	Reference Range
C-reactive protein, mg/dL	1.0	≤0.8
Folate, serum, ng/mL	10.2	>5.9
Hematocrit, blood, %	36	37-47
Hemoglobin, blood, g/dL	12	12-16
Mean corpuscular volume, fL	106	80-98
Tissue transglutaminase antibody, IgA, Serum, U/mL	<0.5 (Normal total IgA)	<4.0 (Negative)
Vitamin B12, serum, pg/mL	162	200-800

the diagnosis in this case include a relative vitamin B12 deficiency with macrocytic anemia and elevated folate levels due to bacterial use of B12 and formation of folic acid. The pathogenesis of diarrhea in SIBO is likely multifactorial secondary to a variety of maldigestive and malabsorptive consequences of bacterial overgrowth.

Celiac disease (answer A), microscopic colitis (answer B), Crohn's disease (answer D), and bacterial infection (answer E) are all incorrect and unlikely causes of diarrhea in this patient.

REFERENCE

Pimentel M, Saad RJ, Long MD, Rao SSC. ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth. *Am J Gastroenterol*. 2020;115(2):165-178. doi:10.14309/ajg.0000000000000501

Question 49

A 62-year-old woman presents to your office for evaluation of diarrhea. She reports 2 months of watery non-bloody painless diarrhea (Bristol Stool Scale, 6) approximately 4 to 6 times daily. She has mild associated nausea without vomiting. She denies antibiotic exposure, travel history, weight loss, vomiting, abdominal pain, rectal bleeding, or melanic stool. There is no change in symptoms with food, and she occasionally experiences 1 to 2 nocturnal stools. She has a history of recently diagnosed type 2 diabetes mellitus and hypercholesterolemia. Her medications include subcutaneous exenatide, aspirin, and atorvastatin. Physical examination reveals a body mass index of 34 kg/

m² but is otherwise normal. Stool testing is negative for *Clostridium difficile* toxin A and B and Giardia antigen.

Laboratory test results are shown below.

Which of the following is the next best step in management for this patient's diarrhea?

- A. Begin cholestyramine
- B. Begin a drug holiday off exenatide
- C. Colonoscopy with random colonic biopsies
- D. Upper endoscopy with duodenal biopsies
- E. Supportive care with oral loperamide and increased dietary fiber

CORRECT ANSWER: B

RATIONALE

This patient's diarrhea is most likely caused by medication, specifically exenatide, a glucagon-like-peptide-1 (GLP-1) receptor agonist. Patients with diabetes are prone to diarrhea due to multiple mechanisms, including small intestinal bacterial overgrowth, autonomic and enteric nervous system dysfunction, dysmotility, dietary factors, concurrent celiac disease, microscopic colitis, and pancreatic exocrine insufficiency. However, it is critical to review these patient's medications at each office visit, as diabetic treatments such as metformin, acarbose, and GLP-1 agonists are common causes of diarrhea. The GLP-1 agonists have been reported to cause diarrhea in 10% to 15% of patients. Once medications are reviewed, any likely causative agents should be stopped if

Laboratory Test	Result	Reference Range
Creatinine, serum, mg/dL	1.6	0.7-1.5
Glucose, plasma (fasting), mg/dL	172	70-99
Hematocrit, blood, %	38	37-47
Hemoglobin A1C, %	7.4	4.0-5.6
Hemoglobin, blood, g/dL	13	12-16
Thyroid-stimulating hormone (TSH), serum, μ U/mL (mU/L)	3.6	0.5-4.0 (0.5-4.0)
Tissue transglutaminase antibody, IgA, serum, U/mL	<0.5 (Normal total IgA)	<4.0 (Negative)

able and monitor for clinic improvement in diarrhea. Only if there is continued diarrhea despite medication cessation or additional concerning clinical factors would further evaluation be necessary (answers C, D). Although supportive care or cholestyramine (answers A, E) can be suggested for mild symptoms, the best next step would be to attempt to stop the likely causative agent, in this case exenatide, monitor for clinical response, and try alternative treatments for glycemic control.

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Selby A, Reichenbach ZW, Piech G, Friedenberg FK. Pathophysiology, Differential Diagnosis, and Treatment of Diabetic Diarrhea. *Dig Dis Sci*. 2019;64(12):3385-3393. doi:10.1007/s10620-019-05846-6

Sun F, Chai S, Yu K, et al. Gastrointestinal adverse events of glucagon-like peptide-1 receptor agonists in patients with type 2 diabetes: a systematic review and network meta-analysis. *Diabetes Technol Ther*. 2015;17(1):35-42. doi:10.1089/dia.2014.0188

Question 50

A 32-year-old woman presents to the office for evaluation of diarrhea. She has 4 to 5 loose non-bloody stools after eating and denies nocturnal diarrhea, recent travel, antibiotic exposure, bleeding, vomiting, or sick contacts. She reports that symptoms began shortly after her Roux-en-Y gastric bypass surgery 3 months ago. She reports that shortly after her meals and especially with liquids, within 15 to 20 minutes, she develops a racing heartbeat, fatigue with desire to lie down, lightheadedness, sweating, and a headache. She then quickly develops loose stool, nausea, abdomi-

nal cramping, and bloating. She has lost approximately 30 pounds since her surgery.

Which of the following is the most likely cause for the patient's diarrhea?

- A. Primary disaccharidase deficiency leading to hyperosmolar small bowel contents and osmotic diarrhea
- B. Reduction in total small bowel absorptive capacity leading to fat and carbohydrate malabsorption
- C. Increased small bowel bile acid concentration leading to bile acid diarrhea
- D. Rapid emptying of hyperosmolar gastric contents into the small bowel leading to plasma fluid shifts with associated vasomotor and hormonal response
- E. Increased small intestinal bacteria concentration leading to maldigestion and malabsorption

CORRECT ANSWER: D

RATIONALE

This patient's clinical presentation is suggestive of early dumping syndrome. Commonly encountered in the post-gastric bypass population (about 25%-50%), dumping syndrome involves altered gastric anatomy and motility leading to rapid emptying of hyperosmolar gastric contents into the small bowel, and subsequent plasma to luminal fluid shifts. These fluid shifts create a sympathetic response and an osmotic diarrhea. Additionally, rapid small bowel distension leads to reflexive enteric nervous mediated bowel contraction. A maladaptive increase in gastrointestinal hormone secretion such as vasoactive intestinal peptide and serotonin, due to bowel distention or fluid contents, also contributes to the symptoms in dumping syndrome. Therefore, diarrhea from dumping syndrome is likely from a combination of osmotic, vasoactive, and hormonal factors.

Symptoms of early dumping syndrome begin within 30 minutes after meals and are often worsened by liquids due to more rapid emptying.

Patients may experience fatigue, weakness, desire to lie down, palpitations, tachycardia, hypotension, lightheadedness, dizziness, nausea, abdominal cramping, and diarrhea. Symptoms generally improve over time after surgery and can be managed by taking small frequent meals low in simple carbohydrates and rich in more complex carbohydrates and protein. Supportive management with antidiarrheals may also help mitigate the symptoms; in severe cases, agents such as octreotide may be required.

Answer A represents lactose intolerance; answer B represents short bowel syndrome; answer C represents bile acid malabsorption; and answer E represents small intestinal bacterial overgrowth. Although post-bariatric surgery patients may experience these alternative causes for diarrhea, they would not be expected to cause such drastic early post-operative vasomotor symptoms and are, therefore, less likely the cause of this patient's symptoms.

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